



ROYAL
PHARMACEUTICAL
SOCIETY



NEW MEDICINES,
BETTER MEDICINES,
BETTER USE
OF MEDICINES

A Guide to the
**Science Underpinning
Pharmaceutical Practice**
May 2014

ABOUT THE ROYAL PHARMACEUTICAL SOCIETY

The Royal Pharmaceutical Society is the dedicated professional body for pharmacist, pharmaceutical scientists and pharmacy in England, Scotland and Wales. We are the only body which represents all sectors of pharmacy in Great Britain. We lead and support the development of the pharmacy profession, including the advancement of science, practice, education and knowledge in pharmacy.

We ensure the voice of the profession is heard and actively promoted in the development and delivery of healthcare policy and work to raise the profile of the profession.

Our mission is to promote and represent the professional interests of our members, supporting the profession to achieve our shared vision for the future. We are committed to supporting and empowering our members to make a real difference to improving health outcomes for patients.

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FOREWORD

The Society leads and supports the development of the pharmacy profession including the advancement of science, practice, education and knowledge in pharmacy, as well as promoting public understanding of pharmacy so that its contribution to the health of the nation is understood and recognised. In addition, the Royal Pharmaceutical Society promotes the profession's policies and views to a wide range of external stakeholders in a number of different forums.

New Medicines, Better Medicines, Better Use of Medicines – A Guide to the Science Underpinning Pharmaceutical Practice represents the views of the Royal Pharmaceutical Society's Pharmaceutical Science Expert Advisory Panel (PS-EAP). The PS-EAP is an independent advisory panel of the Royal Pharmaceutical Society, composed of 17 leading figures in pharmaceutical science from academic, industrial, regulatory, hospital and community practice from across Great Britain. Their remit is to provide strategic direction and assess future developments in pharmaceutical science to the Royal Pharmaceutical Society on critical issues facing pharmacy that impact on patients and the public.

This document is the first to describe, in a single volume, the full spectrum of pharmaceutical science activity and to demonstrate the interdependencies which are critical to the development of new and better medicines and ensure the better use of medicines.

The Guide is aimed primarily at the pharmacy profession and other interested professionals. More targeted guides will be produced from this source material for the public, politicians and other groups. The Guide aims to showcase the important role pharmaceutical science plays in the health and wealth of the nation, in particular demonstrating the breadth of scientific knowledge and understanding necessary to underpin the whole scope of pharmaceutical practice. It also highlights major Challenges and opportunities faced when creating new medicines, improving existing medicines or ensuring the better use of medicines; it makes a series of Recommendations for action from these Challenges. It is intended that the Guide will be a living document, regularly reviewed and updated as appropriate.

Throughout the Guide, examples are given of pharmaceutical scientists who have made significant contributions to their field of work, of medicines developed by pharmaceutical scientists that have significantly improved the lives of patients and new ways in which medicines can be used by patients in safer and more effective ways. It is acknowledged, however, that due to space constraints, it is only possible to include a representative selection of examples.



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- Royal Pharmaceutical Society Industrial Pharmacy Forum
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- Scottish Patients Association
- Society for Biology
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EXECUTIVE SUMMARY

Medicines are one of the most important interventions in modern healthcare. They improve quality of life, reduce the number of life years lost and can avoid premature death. In spite of the ubiquitous nature of medicines, however, the complexity of the medicines development process is often not fully understood.

This Guide summarises the important role pharmaceutical science has played and continues to play in the development and use of medicines and demonstrates the breadth of scientific knowledge and understanding necessary to underpin the full spectrum of pharmaceutical practice. The Guide also highlights the major challenges and opportunities faced when creating new medicines, improving existing medicines or ensuring the better, safer use of medicines, and makes recommendations and calls for action.

Pharmaceutical Science

Pharmaceutical science encompasses the basic, applied and social sciences and plays a part in all stages of the journey of a medicine, from its discovery as a new molecule and formulation as a medicine to its manufacture, approval by the regulatory agencies and ultimate use. Pharmaceutical science in the UK has a long and excellent record of medicines research and development, being at the forefront of many major advances in modern medicines. The ever-changing climate of medicines development and use requires a highly educated, multidisciplinary, flexible and well-trained workforce. UK pharmaceutical science has already made huge contributions to improving the health and wealth of the nation, being a net earner for Britain for more than 30 years. It is an important employer and a leading investor, with £4.85 billion spent on UK research and development in 2011. There are challenges ahead for the industry and it is vital to maintain the UK's position to further advance patient health.

New Medicines, Better Medicines

Developing a new medicine is a costly and lengthy process. It is currently estimated that taking a drug from concept to market requires an average of 12 years with costs in the range of £50 million to over £1 billion being widely reported.

The vast majority of potential drugs never reach market, with most discarded during initial screening. The cost associated with drug failure increases as the drug moves through the development process, with failure in clinical trials frequently costing hundreds of millions of pounds. Both the cost and time taken to bring a medicine to market need to be reduced to ensure the development of new and innovative medicines remains an attractive proposition. New funding mechanisms are needed to incentivise drug development, while at the same time ensuring patients receive the best treatments as early as possible.

This need for new incentives is particularly true for antibiotics as the last new class of drug was discovered in 1987. The incentive for pharmaceutical companies to develop new antibiotics is low due to the poor return on investment they provide. This is because antibiotics are usually taken for a short period of time, are frequently curative and newer drugs will need to be reserved to treat patients with infections which are resistant to treatment by other antibiotics.

Scientific advances are providing exciting new opportunities for drug development. For example, sequencing of the human genome has allowed the development of medicines for specific groups of patients. This approach, known as stratified (or personalised) medicine, has led to the development of treatments such as Herceptin for patients with breast cancer. Advances in systems biology are improving our understanding of how a patient's genes and lifestyle, environmental factors, and the interaction between them, influence both the disease process and its response to a medicine.

These scientific advances allow medicines to be developed for small numbers of patients based on their particular genetic make-up, extend the life of other drugs previously discarded because of poor efficacy and identify new indications for well-established medicines. Increasingly, tests are being developed to measure biomarkers that identify susceptibility to a disease and a patient's likely response to a medicine. Such developments are, however, at a relatively early stage and further research is required if the full potential of these advances is to be exploited.

Many drugs pose significant formulation challenges, including how to selectively deliver drugs to their intended site(s) of action in the body to maximise efficacy and reduce side effects. At present, the vast majority of medicines are given orally. New methods of drug delivery, such as microneedles (small patches consisting of thousands of small needles that pierce the upper layer of the skin), provide examples of where the pharmaceutical and bioengineering sciences have come together and produced practical and economically viable innovations, which should find wide exploitation in the future.

Special formulation issues arise from the complex nature of biologics, for example vaccines, whole cells and even body tissues. Their limited stability means cold storage is needed. This is particularly relevant to vaccinations, where the need for cold storage can account for up to 80% of the price and can prohibit their use in many parts of the world. Another new and exciting treatment area is regenerative medicine where damaged human cells, tissues and even organs are stimulated to repair themselves, thus holding out the promise of a cure for some diseases. One example of this is the use of stem cells to treat failing organs or joints. Further progress in this field will require much research and there are also many ethical issues to be resolved.

While the majority of medicines treat the symptoms of disease, gene therapy offers the possibility of further curative treatments. Although there has been much interest in this field there has only been very limited success and the promise of this form of therapy remains to be realised. To date, the European Medicines Agency has only approved one gene-therapy medicine, Glybera, to treat high levels of lipids in the blood.

Better Use of Medicines

Medicines account for over 12% of the total yearly NHS budget, about £123 billion across Britain in 2011/2012. Once marketed, it is important that medicine use is clinically and cost effective. Between 30-50% of patients, however, taking medicines for chronic conditions do not take them as directed, leading to avoidable ill health and economic loss to the healthcare system and society in general. Research has shown that 6% of UK hospital admissions are related to adverse drug reactions equating to 4% of hospital bed capacity. Patient non-adherence to medication regimens is a complex problem, although

reviewing a patient's medicine(s) and identifying strategies to help them to take their medicine(s) as intended can help improve adherence.

Pharmacists provide evidence-based advice and guidance on medicines to prescribers and patients and contribute to improving health literacy by supplying information that is tailored to an individual patient's needs. Ensuring the best use of medicines, minimising a patient's risk of experiencing adverse events such as side effects, reducing medication errors and contributing to medicines safety are core activities of all pharmacy services. Some pharmacists are now prescribing medicines for patients, with early indications of benefits to patients with chronic conditions.

The nationwide network of community pharmacies, so crucial for the prescribing, supply and use of medicines, could in the future be a place where non-invasive tests for biomarkers are used to aid the early detection of disease and optimise medicine selection.

Children and older people present particular challenges as they require medicines at age appropriate doses and in acceptable formulations. Furthermore, in older people, a balance must be struck between taking many medicines for several conditions and minimising side effects and unwanted drug interactions. In both patient groups there is often insufficient evidence to make informed medicines choices, which is a deficiency that must be addressed.

Pharmaceutical science research has also underpinned pharmacy public health and health protection activities and informed pharmacy policy. Evidence supports the role of community pharmacy in smoking cessation, providing emergency hormonal contraception services and antibiotic stewardship. Further evidence is needed to optimise the sector's contribution to, for example, weight management, alcohol consumption and cancer detection.

In developing countries, much remains to be done to tackle diseases such as HIV-related disease, malaria, and tuberculosis and to control zoonoses. Simple and affordable treatments for diseases endemic in the developing world are urgently required, together with the development of innovative vaccines against these diseases that do not require refrigerated storage.

At a global level, the falsified and counterfeit medicines market must be tackled to ensure such medicines do not enter the legitimate medicines supply chain, potentially causing harm to those who take them.

RECOMMENDATIONS

Throughout this Guide, 71 Challenges are presented which highlight issues faced in creating new medicines, improving existing medicines or ensuring the better use of medicines. Outlined below are the seven Recommendations identified for action, which arise from the Challenges highlighted in the Guide. The Challenges associated with each of the Recommendations are identified by their number in the document. For ease of reference, the full list of all the Challenges is given in section 8.1 of the appendix.

Of the Recommendations given below, only Recommendation 2 deals with a specific group of medicines used to treat disease. This reflects the growing international concerns around the use of antimicrobials in human and veterinary medicines, as well as their use in animals intended for the human food chain, and the impact that a lack of efficacious antimicrobial agents in the future will have on health.

Recommendation 1 – Ensuring the Safe Use of Medicines

- Promote further research into the causes of medication errors in patients and research into interventions to reduce those errors (31, 32, 34, 36, 37, 40, 41, 42, 69)
- Ensure consideration is given to the safe use of medicines at all stages from the discovery of a drug to its administration to a patient as a medicine. (4, 32, 40)
- Improve patient understanding of the risks and benefits of their medication (32, 38, 39, 40)
- Improve pharmacovigilance and reporting of suspected adverse drug reactions by healthcare professionals and patients to identify any safety issues following launch of a medicine (32, 35, 50)
- Encourage developments in toxicology testing, predictive pharmacokinetics, drug delivery, clinical trial design and age-related formulations to aid development of safer medicines (27, 28, 29, 37).

Recommendation 2 – Stimulating New Antimicrobial Development and Improving Antimicrobial Stewardship

- Educate the public and patients on the use of antimicrobials and their place in therapy (45, 46)
- Encourage further development of antimicrobial stewardship by healthcare professionals to maintain the effectiveness of current and any future antimicrobials (45, 46)
- Support the discovery and development of new antimicrobials or treatment methods by developing new financial incentives (2, 13).

Recommendation 3 – Adopting New Technologies

- Educate the public and patients about the ethical and moral issues surrounding the use of new technologies and medicines such as gene therapy, regenerative medicine, therapeutic vaccines and stratified medicine (23, 38, 39)
- Ensure new technologies and medicines fulfil their potential (19, 20, 24, 26)
- Encourage the development of appropriate models of reimbursement to support the use and development of new technologies (18, 25, 63, 64).

Recommendation 4 – Supporting the Development of New and Innovative Medicines

- Encourage the adoption of new technologies and innovative approaches that assist in drug target identification, reduce drug attrition, optimise medicines development and clinical trials, and improve the safety profile of medicines (3, 8, 9, 10, 11, 12, 25, 29)
- Facilitate the supply of new and innovative medicines, and reduce the cost and time to bring these medicines to the patient (2, 6, 14, 16, 17, 18, 20, 21, 22)
- Streamline and reduce the regulatory burden associated with approval, particularly of new and innovative medicines, while continuing to ensure patient safety (15, 25, 58, 63)
- Encourage participation and transparency in clinical trials (27, 65, 66).

Recommendation 5 – Increasing the Evidence Base for Pharmacy

- Increase the health services research expertise within the profession (33, 34, 43, 44, 47, 48, 49, 51, 52, 67)
- Demonstrate the clinical and cost effectiveness of NHS pharmacy services by means of well-conducted, definitive trials that are appropriately funded to enhance the role of pharmacy in the treatment of patients (30, 58, 67, 68).

Recommendation 6 – Supporting Pharmaceutical Science in the UK

- Encourage investment in scientific education and training to ensure a highly skilled and adaptive pharmaceutical science workforce (1, 7, 68, 70, 71)
- Ensure that the UK remains a major player in the development of new and innovative medicines by expanding current Government initiatives aimed at making the UK an attractive location for companies of all sizes (5, 57, 59, 60, 61)
- Increase support for more academic/NHS/industrial partnerships (58, 59, 60).

Recommendation 7 – Improving Access to Medicines at a Global Level

- Tackle disease in developing countries and ensure the equitable access of quality medicines to all patients. (53, 54, 55)
- Support the responsible re-use of medicines and improve access to medicines in developing world communities, thereby improving health. (54, 55)
- Prevent harm to patients by the removal of falsified and counterfeit medicines from the legitimate medicines supply chain and illegal supply through the internet. (56, 62).

The Royal Pharmaceutical Society will lead on the implementation of several of these Recommendations and will work with a range of stakeholders to support the implementation of others. It is envisaged that some of the Recommendations will be achievable in the next few years, while others will require much more sustained effort over many years. An implementation strategy is detailed in section 5 of the Guide.

CONTENTS

FOREWORD	3
ACKNOWLEDGEMENTS	4
EXECUTIVE SUMMARY	6
RECOMMENDATIONS	8
1. INTRODUCTION	12
1.1 PHARMACEUTICAL SCIENCE	12
1.2 MOLECULES TO MEDICINES	13
1.3 MAKING BRITAIN A SAFER PLACE TO TAKE MEDICINES	17
1.4 MAKING THE UK A WORLD CENTRE FOR PHARMACEUTICAL SCIENCE	19
2. NEW MEDICINES, BETTER MEDICINES	21
2.1 DRUG DISCOVERY, DESIGN AND DEVELOPMENT	21
2.1.1 Drug Discovery and Design	21
2.1.2 Drug Optimisation	24
2.1.3 Biopharmaceutics	25
2.1.4 New Antimicrobials	27
2.1.5 Neglected Diseases	28
2.1.6 'New Life' for Old Drugs	29
2.2 DRUG FORMULATION AND DELIVERY	30
2.2.1 Biopharmaceutics and Drug Formulation	30
2.2.2 Low Molecular Weight Drugs ('Small Molecules')	31
2.2.3 Biologics	33
2.2.4 Nanomedicines	34
2.2.5 New and Enabling Technologies	35
2.3 STRATIFIED MEDICINES	36
2.4 PHARMACOKINETICS AND PHARMACODYNAMICS	39
2.4.1 The Younger Population (see also section 3.3.3.1 Younger Patient Groups)	40
2.4.2 The Older Population (see also section 3.3.3.2 Older Patient Groups)	42
3. BETTER USE OF MEDICINES	43
3.1 INTRODUCTION	43
3.2 OPTIMISING MEDICINES USE AND DECISION MAKING	44
3.2.1 Clinical Roles for Pharmacists	45
3.2.1.1 Developing Guidelines	46
3.2.1.2 Medication Review (see also section 3.3.3.2 Older Patient Groups)	46
3.2.1.3 Prescribing	47
3.2.1.4 Self-care and Over-the-Counter Medicines	48
3.3 MEDICINES USE	49
3.3.1 Consequences of Inappropriate Medicines Use	49
3.3.1.1 Concordance	49
3.3.1.2 Adherence Issues	49

3.3.2 Patient Information	51
3.3.2.1 Health Literacy	52
3.3.3 Special Patient Groups	53
3.3.3.1 Younger Patient Groups (see also section 2.4.1 The Younger Population)	53
3.3.3.2 Older Patient Groups (see also section 2.4.2 The Older Population)	54
3.3.3.3 Other Patient Groups	56
3.4 PUBLIC HEALTH	57
3.4.1 Pharmacy and Public Health	57
3.4.2 Health Improvement	58
3.4.2.1 Smoking Cessation, Emergency Hormonal Contraception, Alcohol, Weight Management and Sexual Health	58
3.4.3 Health Protection	59
3.4.3.1 Infection control	59
3.4.3.2 Antibiotics	59
3.4.3.3 Drug Misuse	60
3.4.3.4 Immunisation	61
3.4.3.5 Surveillance of Disease and Medicines	61
3.4.4 Disease Screening	62
3.5 GLOBAL HEALTH	63
3.5.1 Access to Medicines	63
3.5.2 Reducing the Pervallence and Spread of Disease in the Developing World	63
3.5.3 Managing the Health Consequences of Globalisation	65
3.5.4 Effects of Climate Change on Health	65
<hr/>	
4. DEVELOPING THE UK AS A WORLD CENTRE FOR PHARMACEUTICAL SCIENCE	67
4.1 INTRODUCTION	67
4.1.1 UK as the Preferred Location for Pharmaceutical Research, Development and Manufacture	67
4.1.2 UK as the Preferred Location for Clinical Research	71
4.1.3 UK as the Preferred Location for Pharmacy-Focused Health Service Research	72
4.1.4 Funding	73
4.2 WORKFORCE INTELLIGENCE: PLANNING FOR A HIGH QUALITY WORKFORCE	74
4.2.1 Introduction	74
4.2.2 Causes of Workplace Pressures	75
4.2.3 Identifying Future Global Demand for Pharmaceutical Services and Expertise	75
4.2.4 Measurement of the Effectiveness of the Pharmacy Workforce	78
<hr/>	
5. IMPLEMENTING NEW MEDICINES, BETTER MEDICINES, BETTER USE OF MEDICINES	79
5.1 INTRODUCTION	79
5.1.1 World-Leading Pharmaceutical Science	79
5.1.2 Excellent Pharmaceutical Scientists	80
5.1.3 Implementation of the Recommendations	80
5.2 PROPOSED IMPLEMENTATION PLAN	80
<hr/>	
6. REFERENCES	88
<hr/>	
7. GLOSSARY	98
<hr/>	
8. APPENDIX	106
8.1 LIST OF CHALLENGES	106
8.2 LIST OF VIGNETTES	110

I. INTRODUCTION

I.1 Pharmaceutical Science

Pharmaceutical science is the science of medicines discovery, development and use. It is truly multidisciplinary, drawing on many of the basic, applied and social sciences. These skills and knowledge are applied to the discovery, design, formulation, manufacture, regulation and optimal use of medicines, to the ultimate benefit of the patient. By its very nature, pharmaceutical science involves all subject areas that contribute to the study of drugs and medicines and brings together components of many of the sciences, including the chemical, physical and biological sciences, computation, mathematics, statistics and engineering as well as the social and behavioural sciences.

PHARMACEUTICAL SCIENTISTS' KNOWLEDGE

Over the years, pharmaceutical scientists, with their unique blend of knowledge, have played a pivotal role in bringing new medicines to the market: medicines which have improved both the quality of life and reduced the number of life years lost or avoided premature death. It is this distinctive knowledge and understanding that adds considerable value to the development and optimal use of medicines.

As science and medicine have evolved, the required knowledge and skills of pharmaceutical scientists have rapidly expanded in order to keep pace with the latest discoveries and developments. This expansion in the pharmaceutical scientist's knowledge base is expected to continue apace following rapid developments in medical science, particularly in fields such as stratified (or personalised) medicine, regenerative medicine (comprising stem cell therapy and tissue engineering) and nanomedicine.¹⁻⁷

THE ROLE OF PHARMACEUTICAL SCIENTISTS

Medicines have revolutionised the treatment of disease, reduced the need for hospitalisation and surgery, and improved the quality of life of patients. Pharmaceutical scientists have been instrumental in the discovery of new drugs and the development of novel medicines for the treatment of many conditions, including asthma, peptic ulcers, migraines and cancer and in developing new and improved vaccinations.

PHARMACEUTICAL SCIENTISTS' BACKGROUND

Pharmaceutical scientists come from an increasingly wide range of scientific backgrounds. With an emphasis on pharmaceutical science, pharmacy degrees traditionally produced most pharmaceutical scientists. This situation is, however, changing. For example, pharmaceutical sciences degrees are increasingly common, producing graduates with similar pharmaceutical science knowledge to pharmacists but without the training in the clinical components. Other pharmaceutical scientists will have had their original scientific training in a specific specialist discipline (such as chemistry, physics, biological sciences, engineering or the social and behavioural sciences), which they apply to solve pharmaceutical science problems.

Regardless of the route a person has taken, the one common feature of the pharmaceutical scientist is that they apply their unique depth and breadth of scientific knowledge to the problem of improving the development and use of medicines to enhance the lives of patients. Increasingly, this is as part of an interdisciplinary team where the pharmaceutical scientists' breadth of understanding allows them to interact effectively with a wide range of other disciplines and thereby contribute to the medicines development process.

PHARMACY AND PHARMACEUTICAL SCIENCE

In tandem with the expansion in pharmaceutical science as a discipline in its own right, the role of pharmacists working in community, primary care and hospital pharmacy has greatly expanded over recent years and is no longer just about the professional supply of medicines and medical devices to patients. It is now an established role for pharmacists in both primary and secondary care to advise both prescribers and patients about the optimal choice and use of medicines. In some cases, pharmacists select and prescribe a patient's medicines.

The expanding clinical role of the pharmacist has revolutionised the pharmacy profession and has ensured that pharmaceutical science is practised at all stages in the

journey of a drug molecule, i.e. from its discovery through to its use as a medicine by the patient. It is the pharmacist's broad training in the pharmaceutical sciences, combined with knowledge of the evidence base of medicines use, that ensures they are able to contribute to the safe, clinically effective, cost-effective use of medicines. This ensures patients and the public get the best from the medicines they take with minimal risk of adverse effects.

As a consequence of their broad and multidisciplinary knowledge base, pharmacists and pharmaceutical scientists are rightly recognised as experts in medicines and their use. Pharmacists and pharmaceutical scientists play a critical role in ensuring the medicines are produced to the highest quality standards, securing a high level of medicine safety in the UK.

1.2 Molecules to Medicines

DEVELOPING A NEW MEDICINE

The discovery, design, development and manufacture of new medicines and research on their subsequent use in the health service are core activities of the pharmaceutical scientist, while pharmacists in clinical roles directly interact with other healthcare professionals and patients and play an important role in supporting the safe and effective use of medicines. Although medicine development is often viewed as a linear process from drug discovery through to the administration of a marketed medicine to a patient, it is in fact cyclical. Findings from research into the use, safety and efficacy of medicines in patients feed back into the medicines development process and thereby inform and influence the creation of new medicinal products.

Taking a drug molecule from concept through formulation, clinical trials, manufacture and the strict regulatory process to its ultimate use as a medicine by the patient is an expensive, complex and lengthy process with a great many hurdles at which a potential drug may fall. What is not often appreciated is the high rate of attrition, with only a few of the many thousands of molecules originally proposed as drugs getting through the initial screening to the development stage. As the drugs go through the development process, the number of molecules progressing to the later stages of development is greatly reduced with the cost of failure of a drug increasing exponentially. A failure of a drug at a last stage of development in clinical trials can cost hundreds of millions of pounds.

COST OF DEVELOPING A MEDICINE

The development costs of many of the drugs that make it to market will not be recouped. It is currently estimated that taking a drug from concept to market requires an average of 12 years and over £1 billion to do all the research and development necessary before a new medicine can be licensed for use.^{8,9} Currently both the medicines development costs and the system for medicines reimbursement are undergoing, and will continue to undergo, major changes. These changes are a consequence of a variety of different factors including: rapid developments in the underpinning medical science; a greatly improved understanding of the role genetics play in disease; re-structuring in the pharmaceutical industry; an increased number of drugs failing during later phase clinical trials; changes in medicines regulation; and the economic climate. Furthermore, therapies such as gene therapy, which offer the potential of curing a disease, in some cases, after only a few treatments, will require new models of reimbursement due to their high cost and their potential to reduce the cost of ongoing treatment of a patient.

IDENTIFYING DRUG TARGETS

The identification of an unmet medical need and the selection of the disease target(s) are early, key stages in the development of a new medicine. When a target has been determined, a potential drug molecule (known as a 'hit') is tested to assess whether it interacts with the target(s) to produce the desired therapeutic effect.

Increasingly, the synthesis and subsequent screening of molecules against a target are becoming automated, thus potentially allowing an increased rate of throughput. Coupled with this automation, recent advances in the understanding of the human genome and systems biology are expected to reveal hitherto unexplored disease targets, thereby opening up the potential of completely new classes of drug molecules, as well as bringing the concept of stratified medicine much closer to realisation.

SELECTION OF DRUG MOLECULES

The range of potential drug molecules is enormous. Currently, drug molecules range from simple compounds such as the magnesium or aluminium hydroxides used as antacids, through the more 'traditional' and widely used small molecules such as aspirin, large biologics including antibodies and proteins to, in some cases, whole cells as used in stem cell therapy.

Until recently, most new drug molecules were small molecules. Due to changes to the medicines development process, however, relatively fewer new medicines contain 'traditional' low molecular weight drugs. Increasingly, more complicated biologics, i.e. large (biomacro-) molecules, as well as whole cells are undergoing development as medicines. Although this trend is expected to continue, small drug molecules are likely to remain of therapeutic importance. This is because biologics are expensive to manufacture and present a number of technological problems, not the least being that they generally require administration via injection.

With the advent of stratified medicine it is increasingly likely that new applications will be identified for established drugs to treat patients with the appropriate genetic profile, thereby opening up the possibility of being able to treat orphan/neglected diseases.

DRUG DISCOVERY

Once a hit molecule has been identified, the next process is to optimise the hit into a 'lead' compound, which can be developed into a medicine for administration to patients, initially in clinical trials. Frequently hundreds, or even thousands, of derivatives of the hit compounds are synthesised and tested until a lead compound is identified.

MEDICINES DEVELOPMENT AND PRE-CLINICAL TESTING

Once a lead compound has been identified, a decision has to be made as to whether it is possible to develop the molecule into a safe, effective medicine. To do this the compound's physicochemical properties as well as its fate and behaviour in the body all have to be assessed. Particular attention is given to the efficacy and toxicity of the lead compound as these are the main reasons for failure of a compound to progress beyond this stage.

At this stage of a medicine's development, an initial formulation is required for the pre-clinical (animal) toxicology studies necessary to generate the safety data required for exploratory 'first in human' Phase I studies. It is essential to select appropriate animal models for these studies to avoid problems when introducing the drug into man. This is particularly true when the drug is a biologic, where the inappropriate selection of the animal model has led to serious complications when the drug was subsequently introduced into man.¹⁰

FORMULATION CHALLENGES

There can be considerable challenges encountered in the preparation of an appropriate formulation or delivery form of a drug, with the formulation being used for pre-clinical studies unlikely to be the formulation used in man. Indeed, it is not unheard of for a drug to fail at this stage if it does not possess the appropriate physicochemical properties for incorporation into a safe, useable dosage form. Biologics, which are generally administered by injection as opposed to the oral route, bring significant pharmaceutical challenges in terms of their production, characterisation, stability, formulation, delivery, storage and regulation, while whole cells present an even further level of complexity.

Medicines formulation involves the development of preparation methods that reproducibly produce medicines of the desired specification. Specifically the medicines must contain the required drug content, be of suitable quality and exhibit the desired bioavailability and therapeutic performance. The formulation of medicines is a particular expertise of the pharmaceutical scientist. Indeed, altering the way in which a drug is formulated is another way of giving an existing drug 'new life' by changing its pharmacokinetic behaviour. Consideration is increasingly being given to the development of age-specific formulations, acknowledging the different requirements of a medicine in the young and older populations.

PHARMACEUTICAL ANALYSIS

Advances in pharmaceutical analysis have been an important adjunct to the development of new drugs and formulations. It is now commonplace for the physical attributes of a drug and the excipients to be determined to ensure that their behaviour during processing is consistent with a high quality medicine, while modern imaging techniques allow the direct measurement of the intact medicine to ensure manufacturing control. Furthermore, it is becoming possible to identify and quantify ever increasingly small quantities of potentially genotoxic materials, thereby allowing a decision to be made as to whether it is possible to limit the amount of genotoxic material present in a medicine where there is evidence for a threshold-related mechanism. It is now routine for the different isomers of a drug to be isolated to allow the production of medicines that include only the isomer that has the greatest efficacy and/or produces fewer adverse effects.

CLINICAL TRIALS

The clinical development of a new drug traditionally commenced with exploratory 'first in human' Phase I studies to determine preliminary safety, pharmacokinetic and pharmacodynamic profiles of the drug in a small number of healthy subjects: the only exception to this is anti-cancer agents which are only studied in the target population.

As many of the drugs currently in development target specific receptors that are either up-regulated or only present in the disease state, Phase I investigations are increasingly being performed in the target patient group. Indeed, recent developments in understanding the molecular basis of disease are increasingly likely to impact on the clinical development process through the selection of more specific patient populations in relation to their genetic profile and disease categorisation.

DRUG TESTING IN SPORT

One of the world's leading drug control laboratories is the Drug Control Centre at King's College London. The current Director is pharmacist Prof. David Cowan, who, together with Prof. Arnold Beckett, founded and co-directed the laboratory when it opened in 1978, funded by the Sports Council. An important part of the Centre's function is to develop new methods for detecting doping in sport and then apply them to analyse samples from sports competitions. In the lead up to the 2012 London Olympic and Paralympic Games, GlaxoSmithKline funded the Drug Control Centre to help develop new screening techniques that would be world leading in the field of drug testing. The techniques that resulted were announced as super-fast and super-sensitive and allowed the Centre to test over 6000 samples during the Games. Such was the deterrent value of the tests the Drug Control Centre developed that the 2012 London Olympic and Paralympic Games were the cleanest Games ever in terms of drug use. As Prof. Cowan said at the time, "If you cheat – we will catch you." Prof. Cowan was awarded the Pharmaceutical Scientist of the Year Prize by the Royal Pharmaceutical Society in 2013.

If the Phase 1 trials are successful, the drug molecule progresses to Phase 2 clinical trials investigating the efficacy and safety of the drug in a small number (typically 100-300) of patients. It has been estimated that more than 50% of the failures at Phase 2 are due to a lack of efficacy and consequently there is an increased emphasis on predictive tools to improve the drug discovery process. Larger scale Phase 3 efficacy and safety studies follow successful Phase 2 studies. Phase 3 studies are typically multi-centre and multinational and involve thousands of patients. About 2-5% of drugs fail at this stage, leaving the innovator with considerable, unrecoverable expense.

The use of adaptive trial designs, in which the design or analysis of the trial can change as a consequence of interim results, offers the possibility of reducing the time and cost required for the development of new medicines. Adaptive trial designs permit the use of accumulating data to decide how to modify aspects of the study as it continues, without undermining the validity and integrity of the trial. Changes to trials should not be *ad hoc* but 'by design'; and such designs are not a solution for inadequate planning, but are meant to enhance study efficiency. When considering an adaptive trial design the feasibility, validity, integrity, efficiency and flexibility of the proposed study and its objectives should be assessed. These designs are appealing when credible responses can be observed at an early stage and in the right circumstances can improve safety and patient outcomes without compromising statistical validity. The ongoing assessment of sample size avoids under or over allocation of patients when statistical power is based on the assessment of a critical variable. Fewer patients are then exposed to a less effective therapy, more data are collected on effective therapy and fewer subjects are required to achieve the objectives. The study is safer and more efficient in terms of time and cost.

DRUG SCALE-UP AND MEDICINES MANUFACTURE

Going from small-scale to large-scale manufacturing is a major undertaking. Initial scale-up of drug synthesis and medicine manufacture generally starts before clinical trials commence because of the large quantity of drug required to manufacture the medicine for use in clinical trials. The process of bulk manufacture typically starts about six months to a year before the first application is submitted to the regulatory authorities.

As the manufacturing process is different from drug to drug or biologic to biologic, companies often need to build a new manufacturing facility or alternately sometimes reconstruct an old one. Furthermore, the formulation selected for a medicine may also require a new production facility to be built. Regardless, each facility must meet strict, regulatory guidelines for Good Manufacturing Practices (GMP). Making a high-quality drug or biologic or manufacturing a medicine on a large scale requires considerable expertise. Indeed, there are few, if any, other industries that require such a high skill level when manufacturing their product.

REGULATORY APPROVAL AND MEDICINES USE

The results from all pre-clinical and clinical studies are submitted to the regulatory agencies for approval and granting of a marketing authorisation (previously a product licence) to allow the medicine to enter the market. The regulatory agencies also play an essential role in safeguarding public health through carrying out inspections of sites involved in the discovery, development and manufacture/production of drugs and medicines as well as sites involved in animal toxicity and human clinical studies.

Despite the rigorous medicine development process, however, unexpected safety issues can still arise after medicines are authorised, particularly if used outside the marketing authorisation or when taken with other medicines. As a consequence, once launched, post-marketing surveillance (i.e. pharmacovigilance) and further clinical trials are undertaken along with research to ensure the acceptable safety of the medicine and to assess its place in the treatment of patients, e.g. pharmacoepidemiological studies and clinical research.

HEALTH SERVICES RESEARCH

In addition, health services research is required to identify the place of the new medicine in health policy, public health and in medicines utilisation. Research is also needed to determine how patients perceive and use the medicine, all of which can feed back into the medicines development process to inform and influence the development of new medicinal products.

In each of these steps, pharmaceutical scientists play an important role in ensuring the necessary data and information are produced to enable a drug molecule or medicine to progress to the next phase. This is especially true in the design of medicines and their manufacture to the highest quality standards, where the multidisciplinary expertise of the pharmaceutical scientist comes to the fore.

CHALLENGES

1. *Ensure excellence in the development of medicines by fostering and promoting world-leading pharmaceutical science*
2. *Reduce the time and cost to market of a medicine*
3. *Understand the target population better to develop better, safer and more effective medicines*

1.3 Making Britain a Safer Place to Take Medicines

Medicines are undoubtedly the most common intervention received by a patient, although what is not widely recognised is that no medicine is ever completely safe. As already shown, pharmaceutical scientists and pharmacists, along with other healthcare professionals, play an important role in ensuring the acceptable safety of a medicine. This is both during the formulation and manufacturing stages and during the review of the data (including clinical trial data) submitted to the regulatory agencies as part of the approval process. This next section considers the role pharmacists and pharmaceutical scientists also have in ensuring the safety of a medicine once it has been approved for use.

ADVERSE EVENTS TO MEDICINES

Adverse events associated with medicines can cause harm. In one study, 6% of all patients admitted to hospital, over a six month period, were admitted due to an adverse drug reaction. 70% of these were thought to be avoidable.¹¹ Given the level of patient harm and suffering caused by adverse drug events, as well as the huge financial burden they place on the NHS, it is not surprising that reducing adverse drug events and other patient safety incidents are a priority for the UK Government. This is demonstrated by the number of policy documents and reports which focus on this issue. National patient safety initiatives have been put in place, including the English Patient Safety First Campaign,¹² the Welsh 1000 Lives Plus Campaign¹³ and the Scottish Patient Safety Programme.¹⁴

IMPROVING THE SAFE USE OF MEDICINES

Improving the safety profile of medicines and ensuring their safe use are areas in which pharmaceutical scientists, particularly pharmacists, continue to play an important role. This role involves the detection, recording and reporting of suspected adverse drug events. Pharmacists also contribute to reducing medication errors during the stages of prescribing, preparation, administration and monitoring of medicines. They can minimise adverse

events to medicines, address adherence issues and optimise medicines use. These roles will undoubtedly increase in the future as the proportion of people over 65 with multimorbidity and on polypharmacy regimens increases.

Pharmacists and pharmaceutical scientists have been instrumental in implementing guidance from the policy documents mentioned above. Much work has already been undertaken to reduce the potential problems associated with the use of high-risk medicines such as heparin, warfarin, insulin, lithium, opioid analgesics, methotrexate and potassium-containing injections. In addition, improvements have been made to the process of administration of high-risk medicines such as intrathecal injections and on the safer use of injectable medicines, infusion devices and syringe drivers.¹⁵

MEDICATION ERRORS

Research into the causes of medication errors, adverse drug events and non-adherence to medicines by patients has increased understanding of the often complex and inter-related factors involved. It is known that the number of items dispensed in a pharmacy has been steadily increasing in recent years and that the potential for medicines errors in the dispensing process increases as workloads increase. A greater acceptance of a safety culture that encourages open discussions around errors and near misses, rather than the traditional 'blame culture', is required to ensure learning from mistakes, so that similar errors do not occur in the future.

MEDICATION ERRORS

Medication errors are one of the leading causes of injury to patients, leading to increased morbidity and mortality as well as an economic burden to health services. The 'gold standard' for assessing the clinical significance of medication errors was developed by pharmacist Professor Briony Dean Franklin. For nearly 20 years, Prof. Franklin has been involved with medication safety research and has published widely in this field. Professor Franklin is currently Professor of

Medication Safety at the UCL School of Pharmacy and Director of the Centre for Medication Safety and Service Quality (CMSSQ), a joint NHS and academic research unit. These roles allow her to combine her interests in research, education and training, and hospital clinical pharmacy practice. In recognition of her research into medicine safety, Prof. Franklin was awarded the Royal Pharmaceutical Society's Practice Research Medal in 2005.

REDUCING MEDICATION ERRORS

While there has been success in reducing patient medication errors, there is still place for improvement. The use of automation, or pharmacy robots, in medicines dispensing activities in a pharmacy is slowly increasing as it offers improvements in both efficiency and accuracy of the dispensing process. Evaluations of robotic systems implemented in UK hospitals have shown decreases in medication selection error rates, which contributes to safer patient care and reductions in preventable harm to patients. Robotic systems also have the potential to allow more time to be allocated to providing other services directly to patients.

There is a need for improved reporting of patient safety incidents, by both health professionals such as pharmacists and patients themselves. There is a requirement for greater shared learning from mistakes. There must be increased implementation of solutions that will prevent future harm and ensure the risk to patients taking medicines is as low as possible. Care must be taken, however, to ensure that any solution introduced to address one type of error is not associated with the emergence of other error types.

In most situations prescribers are encouraged to prescribe medicines using the generic name of the drug to reduce the cost burden on the NHS. In a few specific instances, however, it is safer to prescribe branded products as due to the molecular complexity of the product there is a lack of therapeutic equivalence

between products. Examples of medicines that should be prescribed by their brand name include tacrolimus, ciclosporin and several antiepileptic products, some modified-release preparations, as well as biosimilars.

MEDICINES RECONCILIATION

Medicines reconciliation is increasingly recognised as a way to improve the safe use of medicines. It is particularly important when patients move between settings, either within healthcare or between healthcare and social care environments.¹⁷

Through accurate medicines history taking, medicines reconciliation identifies an accurate list of a patient's medicines, ensures the medications and doses are appropriate and records any changes in prescriptions. By assessing previous and current prescriptions, any discrepancies in a patient's medicines are reconciled.

Pharmacists and pharmacy technicians are involved in several of the steps in the medicines reconciliation process, particularly in ensuring that on admission to hospital, and at transfer of care, the patient's medicines history is accurate and that any errors or discrepancies are investigated. This process ensures that accurate information on a patient's medicines is communicated to healthcare professionals involved in the care of the patient, thereby reducing the risk of medication errors and adverse drug events.^{18,19}

AN INCREASED ROLE FOR PHARMACISTS

Pharmacists' knowledge of pharmacology and therapeutics has long been acknowledged. The patient safety agenda has led to an increased and defined role for pharmacists providing cognitive advice on medicine selection and use, whilst maintaining their role in the technical aspects of safe medicines, distribution, supply and use. These roles include, but are not limited to,

clinical pharmacists working in hospital, primary care and the community, providing prescribing advice, advice to decision makers at organisational and individual level and patient facing roles, including prescribing, in all three settings.

CHALLENGE

4. *Ensure patient safety: from drug discovery to medicines administration to patients*

I.4 Making the UK a World Centre for Pharmaceutical Science

BENEFITS OF THE PHARMACEUTICAL INDUSTRY

The UK has had a long history of and an excellent record in pharmaceutical science research and development, being at the forefront of many of the major advances in medicines. It has considerable strengths in the areas of drug discovery, pharmacology, pre-clinical research including formulation and early clinical pharmacology and toxicology. Both the UK pharmaceutical industry and academia have been extremely effective at discovering highly successful drugs, which the pharmaceutical industry then develops into medicines suitable for patient use. In addition to improving the health of the nation, the pharmaceutical industry has been a major contributor to the nation's wealth. It has been a net earner for Britain for more than 30 years, a significant employer and the leading investor; investing £4.85 billion in UK research and development in 2011.²⁰

RE-ORGANISATION WITHIN THE PHARMACEUTICAL INDUSTRY

The UK pharmaceutical industry is, however, undergoing major re-organisational changes and, as a consequence, is in serious danger of losing its position as a leader in the pharmaceutical sciences. The changes in the pharmaceutical industry are reflected in the nature of the companies in which pharmaceutical scientists are employed. While the number of people directly working in the pharmaceutical industry has remained steady over the last 15 years at a total of 72,000, with 27,000 working in research and development, the distribution of employees between large companies and small and medium-sized enterprises (SMEs) has changed. The number employed in large companies is decreasing and the number in SMEs increasing.^{21,22}

SUPPORTING THE PHARMACEUTICAL INDUSTRY

It is essential for the competitiveness and health of the UK that its pharmaceutical industry remains strong. In this challenging environment, various Governmental initiatives, such as the Patent Box, the Innovation Platform and the UK Intellectual Property Office consultation on proposals to change the UK's copyright system, have been put in place to try to ensure that the UK retains its position at the forefront of major advances in medicines. These initiatives need to be regularly monitored to see if they are achieving their intended aims and, if necessary, modified to ensure reinvigoration of the UK pharmaceutical industry. Additionally, specific measures need to be in place to allow the many small and medium-sized pharmaceutical enterprises that currently exist in the UK to flourish in the present economic climate. Furthermore, the regulatory authorities, conscious of the damage that bureaucracy and regulatory barriers can do to innovation, development and approval times, have introduced initiatives aimed at improving timings, reducing delays, removing bottlenecks and minimising unnecessary and inconsistent checks at both national and European level.

ADVANCING DRUG DISCOVERY

The discovery of sumatriptan, the first in a new class of drugs for the treatment of migraine, has been described as the most important achievement in the treatment of headache in the last 50 years. It was Dr Pat Humphrey's work on cerebrovascular pharmacology that led to the development of sumatriptan. Dr Humphrey, a pharmacy graduate, had joined Allen and Hanbury's in 1972, becoming Director of Pharmacology at Glaxo in 1983. Dr Humphrey was also instrumental in the discovery of several

other drugs, including naratriptan (migraine), alosetron (symptoms of irritable bowel syndrome), ondansetron (nausea and vomiting) and salmeterol (asthma). More recently, as Founder and Head of Research at Theravance (US), and through his involvement with Verona Pharma PLC, Dr Humphrey has continued his involvement in the discovery of new drugs. In recognition of his work, Dr Humphrey has received many awards, including the Royal Society's Mullard Medal in 1997 and an OBE for his services to migraine research.

DEVELOPMENTS WITHIN THE PHARMACEUTICAL INDUSTRY

The pharmaceutical industry itself also needs to continue to be innovative, changing some of its more established practices to be more responsive. For example, the industry could gain great benefit from the development of new innovation models and an understanding of how best to share (pre-competitive) knowledge and costs among collaborators at other pharmaceutical companies. In addition, Academic Health Science Centres (AHSC), i.e. partnerships between universities and hospitals in England, have the goal of ensuring that breakthroughs in medical research lead to clinical benefit for patients. Academic Health Science Networks (AHSN)²³ have recently been established in England with a core function of engaging the NHS with research to drive innovation in the NHS to improve the health of the nation and to create wealth for the economy.

HEALTH SERVICE RESEARCH

Through their involvement in health service research, UK pharmacy practice researchers have provided the evidence necessary to support many of the services that are now core to community pharmacy. To further increase the impact of research, adequate funding to enable the large scale intervention studies necessary for evidence-based decision making to be carried out is required, together with closer working with other academic disciplines. Furthermore, to increase the amount of research carried out, the research capacity of the pharmacy profession must expand to the position where, ideally, research is considered a core activity of community and hospital pharmacists.

PHARMACEUTICAL SCIENCE WORKFORCE

In order to maintain and expand a strong pharmaceutical industry, a constant supply of well-trained and knowledgeable pharmaceutical scientists is required. There is also a need to incentivise scientists to study subjects where there is a serious skills shortage, such as pharmacokinetics and pharmacodynamics.²⁴

Capacity building (as noted in section 4.2) is also important and essential for maintaining the pipeline of academic and practice-based leading researchers, so that the UK can retain its leading role in pharmacy practice research. By forming partnerships with universities and the new AHSN and AHSC, the newly established Pharmacy Research UK has a central role in this agenda.

Research and information to support workforce planning is vital in making a case for resources. Although evidence does exist on the NHS pharmacy workforce, comparable information on pharmaceutical scientists is lacking – a shortcoming that needs to be addressed. This is especially important if the UK is to maintain its strength and leading position in pharmaceutical science.

CHALLENGES

5. *Secure and strengthen the UK's position as a major player in the global pharmaceutical industry*
6. *Build upon academic-hospital-industrial and industrial-industrial partnerships to develop new and innovative approaches for drug discovery*
7. *Encourage new Government initiatives to support the UK science base*

2. NEW MEDICINES, BETTER MEDICINES

2.1 Drug Discovery, Design and Development

Increasingly, drugs are being identified that have the potential not only to prolong life but also inhibit and cure disease processes, giving patients a better quality of life for longer. These developments in drug discovery look set to continue apace in line with the rapid improvements in the understanding of disease processes, the influence of

genetics provided by systems biology and systems pharmacology, and an understanding of the human genome. Pharmaceutical science must harness these advances to ensure that patients get the best possible medicines to treat their particular disease.

2.1.1 DRUG DISCOVERY AND DESIGN

The first stage in medicines development is drug discovery, the goal of which is to find a promising molecule (the 'hit' compound) that acts against the target and could potentially lead to the development of a new medicine.

IDENTIFYING HIT COMPOUNDS

Up until the 1980s, hits were typically found through testing chemicals from natural product materials isolated from selected plants, bacteria and fungi (frequently those with a pertinent history of use in traditional medicine).²⁵ Antibiotics such as penicillin and streptomycin were discovered in this way. In fact, natural products still

constitute a rich source of new drugs, with ciclosporin, paclitaxel and artemisinin being isolated from a fungus, an endophytic fungus and a herb, respectively. Over the last few years, researchers have found drug hits using more exotic organisms than have been previously exploited, such as insects and Caribbean sea sponges – the latter providing many C-nucleoside analogues in use and in development trials as anti-cancer agents.²⁶ Increasingly, animals such as frogs and snakes are being explored as potential sources of new drugs to treat a variety of diseases.^{27,28} It is expected that natural products will continue to be a source of new drugs in the future.

DEVELOPMENT OF A NEUROMUSCULAR BLOCKING AGENT FOR USE IN ANAESTHESIA

In surgical procedures it is often necessary to relax the body muscles, particularly in the abdomen. Although this can be achieved with some of the dart and arrow poisons used by aboriginal hunters, these poisons result in a long-lasting muscle paralysis, including the diaphragm, so that the patient cannot breathe unaided. Prof. John Stenlake, a graduate of the London School of Pharmacy working at Strathclyde University, secured a Medical Research Council grant to investigate the preparation of shorter-acting muscle relaxants by a mechanism known as Hofmann elimination. Pharmacist Dr Roger Waigh was initially employed

on the grant, but quickly showed that the original rationale would not work. He found an alternative which led to synthesis of a series of highly active relaxants, prepared under his supervision first by Dr John Urwin, a pharmacist from Nottingham University, and then by George Dewar, another pharmacist from Strathclyde University who prepared atracurium as part of his PhD studies. For several years, atracurium was the market leader worldwide and is still used for long operations, particularly in the elderly. On behalf of the group, Professor Stenlake was awarded the Mullard medal of the Royal Society.

Since the 1970s, pharmaceutical scientists have used their expertise in chemical synthesis to generate huge libraries of molecules to screen against potential drug targets. High throughput screening (HTS) – a technique to experimentally test the large numbers of molecules in these libraries – has enabled more hits against clinically relevant targets to be identified, although thus far HTS has, perhaps surprisingly, not resulted in an increased number of successful drug candidates.²⁹

STRUCTURE-BASED DRUG DISCOVERY

Structure-based drug discovery has advanced rational drug design significantly. It relies on knowledge of the three dimensional structure of the target receptor or enzyme on which the drug is required to act, which is generally obtained by X-ray crystallography. Knowing how a hit molecule binds to the pharmacological target can prove invaluable when exploring ways in which to modify the hit to make a better fit with the target. Many modern drugs on the market, particularly the anti-cancer kinase inhibitors, have been developed using this process.³⁰

Structure-based drug discovery is not a new concept. For example, preparing new molecules, which are similar

in structure/properties to endogenous ligands, has been used to successfully drive drug discovery programmes. Indeed, this knowledge-based rational approach was very successfully exploited in the 1970s to develop beta-blockers to treat cardiovascular disease by opposing the action of adrenaline and H₂-antagonists to treat stomach ulcers by interacting with histamine receptors. Both these classes of drugs revolutionised drug discovery and heralded the era of the 'blockbuster drug'.

More recent advances in technology have complemented this structure-based approach. Fragment-based drug discovery, for example, uses X-ray crystallography or NMR spectroscopy to identify appropriate chemical building blocks from a fragment library that interact with the target. These fragments can then be combined synthetically to generate more potent and selective molecules that occupy the whole binding site.³¹

Further understanding of disease processes and the influence of genetics thereupon, coupled with improvements in analytical methodology and computer technology, will undoubtedly lead to ever more sophisticated approaches to the identification of hit molecules.

REVOLUTIONARY NEW DRUG THERAPIES

Glaxo was transformed from unglamorous beginnings as a producer of powdered milk for infants into one of the world's largest and most profitable manufacturers of prescription medicines by pharmacist Sir David Jack and his team. Sir David joined Allen and Hanbury's as head of research in 1961. He considered that Glaxo's traditional strategy of licensing drugs from foreign companies was unsustainable in an increasingly global industry and that the treatment of common disorders, that robbed patients of a good quality of life, had to be tackled as a matter of priority. His team therefore concentrated on treatments for respiratory, cardiovascular and gastrointestinal tract diseases. Sir David's first success was the

discovery of the bronchodilator salbutamol in 1966, a new effective asthma rescue therapy launched as Ventolin in 1969. A decade later, in May 1976, his team produced ranitidine hydrochloride, a treatment for gastric and duodenal ulcers. A supremely efficient development programme followed, lasting just five years, and Zantac was launched in 1981 to become the first 'blockbuster' drug, generating sales of over \$1 billion annually. Sir David was recognised with a CBE in 1982, the Royal Society's Mullard Medal in 1991, an FRS in 1992 and a knighthood in 1994 for his services to patients and commercial success of his scientific and strategic brilliance.

VALIDATING DRUG TARGETS

The key to success in any drug discovery programme continues to be validation of the drug target, i.e. establishing whether the target is clinically relevant so that, when activated by the putative drug (whether a small molecule or biologic), the desired clinical effect is produced. Identification of appropriate biomarkers that indicate whether the drug is likely to work in the anticipated way is also crucial to any drug discovery programme.

Recent advances in molecular biology and biotechnology are revolutionising the approach taken to identify enzymes and receptors to be targeted clinically. As a consequence, pharmaceutical companies are increasingly moving away from mass screening to exploiting DNA microarray analyses, proteomics, systems biology and systems pharmacology. These techniques are used to investigate how acquired and inherited diseases alter a cell's gene and protein expression profiles, thereby identifying suitable targets for therapeutic intervention to drive scientifically-based, rational drug design.

Recent advances in systems biology have also renewed interest in determining whether rare diseases are linked to single gene defects, which may permit the underlying mechanism for the disease to be characterised.

Identification of these single gene defects may enable links to be made to similar underlying mechanisms for more common diseases, which may also provide new targets to feed into the drug discovery process.³² Although there has been an expectation for some time that mapping the human genome would revolutionise the diagnosis, prevention and treatment of human disease, only now is this promise starting to be realised in terms of production of new medicines. One of the reasons why genomics has yet to have its full impact on patient therapy is because of the mistaken premise that all illness is solely genetic, neglecting the substantial, and indeed complicating, role played in some diseases by environmental and lifestyle factors such as diet and smoking.³³

CHALLENGES

8. *Improve the drug discovery process by effectively harnessing new information and technologies*
9. *Improve methods to correlate target validation with desired clinical outcomes*
10. *Identify the genetic defects associated with specific diseases and the role of genetics, the environment and lifestyle on disease development*

DEVELOPMENT OF ANTI-CANCER MEDICINES

The discovery and development of new anti-cancer drugs with novel chemical structures and/or modes of action is essential for improving the treatment of cancer. Professor Malcolm Stevens has successfully used his pharmaceutical science knowledge to create new anti-cancer drugs that possess three qualities, namely a novel mechanism of action, an ease of synthesis and a pharmaceutical robustness. Using this approach, Prof. Stevens has been responsible for taking several new experimental cancer drugs into the clinic, two of which reached the market, namely: bropirimine (Remisar), an immunomodulatory and antiviral agent which triggers cytokine cascades and temozolomide (Temodal) which is primarily used to treat glioblastoma, the most common adult brain tumour. Total worldwide

sales of Temodal (without generic versions) have exceeded \$8.5 billion. In line with Prof. Stevens' philosophy in creating new anti-cancer drugs, temozolomide possesses three qualities: an ability to change gene expression through selective methylation of DNA, synthesis using a two-stage process and oral administration at out-patient clinics. Indeed, the commercial synthesis is the original synthesis developed in 1980 by PhD pharmacist Robert Stone. In recognition of his outstanding contribution to cancer research, Prof. Stevens has received many awards, including the 1994 Royal Pharmaceutical Society's Harrison Memorial Medal, an OBE in 1999 for his achievements in anti-cancer drug design and an FRS in 2009.

2.1.2 DRUG OPTIMISATION

IDENTIFYING LEAD COMPOUNDS

Once a hit molecule has been identified against a validated drug target, this is only the beginning of the drug development process. The next stage in the process involves optimising the hit into a lead compound (and ultimately a pre-clinical candidate for clinical trials in patients) that meets the specific criteria required for development to proceed. Identifying the hit generally relies on a molecule producing activity in an assay with the target in solution (an *in vitro* assay). The lead compound has to replicate its activity against the target in cells, then ultimately in animals (to test for safety, efficacy and toxicity) before being administered to healthy volunteers. It must also navigate the issues surrounding absorption after administration, distribution, metabolism and excretion to maintain sustainable concentrations in the blood to produce the desired clinical effect. Hundreds of derivatives of the hit compound will be synthesised in order to address all of these lead optimisation challenges until, ultimately, one compound is identified that has potency against the target in a living system for a sustainable time frame (often referred to as efficacy). Once such a candidate molecule is identified (and often they are not for a variety of reasons), planning for clinical trials in humans can begin.

DRUG SYNTHESIS

The methods employed to synthesise drug substances are set to change in the future, with the major driver being the desire to use safe, sustainable and economically viable processes, capable of delivering high yields of the desired molecules and ideally having a process efficiency that approaches 100%. Such goals are presently sought through the use of flow chemistry and micro-reactors and through synthetic biology, the latter involving either the engineering of enzyme synthetic pathways within micro-organisms or artificial cells to generate the desired molecules.

CHALLENGES

11. *Produce reliable and predictive physiologically-based pharmacokinetic modelling techniques to optimise a hit-to-lead process*
12. *Increase the likelihood of developing a medicine by optimising its absorption, distribution, metabolism, excretion and toxicity*

CONTINUOUS MANUFACTURING

The Centre for Continuous Manufacturing and Crystallisation (CMAC) is a major new initiative aimed at accelerating the adoption of fully continuous manufacturing processes for the quicker and more sustainable production of high-value, higher-quality chemicals such as pharmaceuticals at lower cost. To achieve this goal, CMAC's Director, pharmacist Professor Alastair Florence of the Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, leads a multidisciplinary team of academics from seven British universities. The team harnesses expertise from a wide range of scientific disciplines, including chemical and

process engineering, chemistry, pharmaceutical science as well as manufacturing and operations management from across academia and industry. To date, CMAC has raised over £60 million from the Engineering and Physical Sciences Research Council together with input and support from CMAC's founding pharmaceutical industry partners, GlaxoSmithKline, AstraZeneca and Novartis. In recognition of his achievements, Prof. Florence was awarded the Royal Pharmaceutical Society Science Medal (2004) and was Conference Chair for the Academy of Pharmaceutical Sciences 2013 UKPharmSci conference.

2.1.3 BIOPHARMACEUTICS

TYPES OF BIOLOGICS

A major change is occurring in the field of drug discovery in that the typical low molecular weight drug molecules are being increasingly supplemented by biologics (or biological products). Biologics are therapeutic agents often obtained from a variety of natural sources (bacteria, yeast or increasingly mammalian, including human, cells) and include 'living entities' such as cells and tissues. As with classical low molecular weight drugs, many biologics treat the disease, although others are used for prevention or diagnosis. Most biologics are large complex molecules or mixtures of molecules, many times the size and molecular weight of their 'small' drug counterparts, making their analytical characterisation extremely difficult. There are many examples of biologics, including proteins such as the hormone insulin (the first biologic), monoclonal antibodies, blood proteins such as tissue plasminogen activators, cytokines such as interleukins, the nucleic acids, DNA, siRNA and antisense oligonucleotides, vaccines, and cells and tissues.

MANUFACTURE OF BIOLOGICS

Although some biologics such as peptides and oligonucleotides are prepared by solid-phase synthesis, many biologics are produced by biotechnology and other cutting-edge techniques; their manufacture is a very complex and expensive process requiring many specific isolation and purification steps. More robust processes are required to make the manufacture of biologics more efficient, predictable and flexible. These include reducing batch variability, minimising the risks of contamination, particularly viral contamination and using platform processes, where a single process can be used for the manufacture of several different products.

The complexities of biologics manufacturing, coupled with manufacturing protocols being generally proprietary knowledge, make it virtually impossible to prepare an exact copy of a biologic.^{34,35} As a result, copies of innovator biologics are termed biosimilars. In fact, the manufacturing process for a biologic is often considered to define the product as any change in the manufacturing process can lead to changes in safety, quality and efficacy and produce a different end product. Consequently there are many technological and regulatory issues that must

be addressed to facilitate the development of new biological agents, and biosimilar agents, into new medicines.³⁶ This situation is in contrast to that of low molecular weight drugs where the drug molecule used in a generic medicine is identical to that used in the innovator product.

The analysis of biological molecules presents particular difficulties in controlling the batch-to-batch variability of products. The patents of recombinant therapeutic proteins and polypeptides such as insulin, human growth hormone, interferons and erythropoietin have now expired and biosimilar products are becoming available. Assessing the differences between innovator and biosimilar products now requires substantial additional data to that required for generic products containing low molecular weight drugs and is a real challenge for pharmaceutical analysis.

ROLES OF VACCINES

An important tool in the pharmaceutical armamentarium is the vaccine. Vaccines are biological products that provide immunity towards disease. Unlike the other therapies described above, vaccines are generally prophylactic as they are intended to prevent or ameliorate the effects of a future disease – frequently an infection but also more recently cancer – rather than treat it. Vaccines have been responsible for the eradication of smallpox and reducing the incidence of polio, measles, chickenpox and typhoid. Unfortunately, it is not easy to prepare a vaccine against every virus and bacterium. It is particularly difficult to produce vaccines against rapidly evolving micro-organisms such as HIV or micro-organisms that cannot be readily treated with antibodies alone and which require the involvement of other immune cells. For this reason, new tuberculosis (TB) vaccines are required.^{37,38}

TYPES OF VACCINES

The production of new vaccines is a very important area of research. Recently, vaccines produced from the human papilloma virus have been introduced for the prevention of cervical cancer precancerous lesions and genital warts and is administered to young females. Furthermore, therapeutic vaccines to treat patients already with a disease such as HIV or cancer are attracting much interest. Indeed, the US Food and Drug Administration (FDA) has approved glatiramer acetate for treatment of multiple sclerosis and sipuleucel-T for use in men with metastatic prostate cancer. Glatiramer acetate is a synthetic vaccine composed of the acetate salt of four polypeptides that stimulate myelin basic protein, while sipuleucel-T is the first cellular immunotherapy. As with vaccines to prevent infection, the goal of a therapeutic vaccine is to stimulate the host's immune system to destroy the causative agent of the disease.

REGENERATIVE MEDICINE

Regenerative medicine offers the exciting possibility of replacing damaged tissues and organs in the body and/or stimulating the body's own repair mechanisms to heal previously irreparable tissues or organs. In contrast to conventional drug treatments, which tend to address only the symptoms of disease, regenerative medicine has the potential to tackle the underlying causes of the disease and thereby cure the disease.

Tissue engineering, a component of regenerative medicine, is where organs or tissues are grown *in vitro* and transplanted into patients. Three-dimensional tissues are made by implanting cells into scaffolds composed of natural or biodegradable materials. Exposure of the cells to the correct growth factors, nutrients and stimuli enable the cells to grow and divide, taking the shape of the scaffold. Once transplanted into patients, the scaffold dissolves with the cells now taking the form of the tissue to be replaced. Tissue engineering has successfully produced several tissues such as bone, cartilage and skin and has potential applications in many diseases. Further progress in the field will require greater understanding of the mechanisms of tissue differentiation, as well as standardisation of processes and resolution of ethical issues.

REGENERATIVE MEDICINE

Regenerative medicine, i.e. replacing or regenerating human cells, tissues or organs to restore or establish normal function, holds the promise of regenerating damaged tissues and organs in the body. Pharmacist Prof. Molly Stevens of Imperial College, London undertakes research into the directed differentiation of stem cells, the design of novel bioactive scaffolds and new approaches towards tissue regeneration. To date she has developed novel methods for engineering large quantities of human mature bone for autologous transplantation as well

as other vital organs such as liver and pancreas. Efforts to commercialise the technologies have led to spin-out companies and the setting up of a clinical trial for bone regeneration in humans. Amongst the many awards Prof. Stevens has received is the Royal Pharmaceutical Society's 2007 Conference Science Medal. In 2004, she was recognised in the TR100 (the top 100 Young Innovators under the age of 35 who were transforming technology), while in 2010 she was named by The Times as one of the UK's top ten scientists under the age of 40.

STEM CELL THERAPIES

While stem cell research holds tremendous promise for the treatment of many serious diseases, a large number of issues exist around the use of stem cells. For example, in addition to the moral and ethical issues raised by the use of embryos, stem cell therapy has a number of other challenges, including contamination, genetic instability and cancer risk. While the concept of using human cells to treat disease is not new – blood transfusions and organ transplants have been performed for many years – it is only over the past 20 years that developments in research have enabled cell therapy to become a real possibility for a wide range of conditions.

The first human clinical trial for a stem cell therapy (to treat spinal cord injuries) was approved by the FDA in early 2009. The first stem cell therapy to be approved by the FDA was in 2011 and was used to treat patients with disorders affecting the haematopoietic system such as certain blood cancers.³⁹ While stem cell therapies might

not at first glance be thought of as a drug, the FDA classified them as drugs in 2012 and thus the term stem cell drugs is gaining acceptance.⁴⁰ There is also the need to define the regulatory requirements and approval pathway required for clinical trials with stem cells and stem cell-derived products.

It looks highly probable that low molecular weight drugs will be used in the future to stimulate adult cells to revert to their embryonic state *in situ*, thereby avoiding the need to administer stem cells directly. It has been reported recently that the low molecular weight, anti-diabetic drug metformin can activate stem cells to generate new neurons and other brain cells, thereby providing hope of a means to treat brain injuries and even neurodegenerative diseases such as Alzheimer's disease.⁴¹ The use of low molecular weight drugs *in situ* to achieve the same ultimate effect as stem cell drugs has a number of obvious advantages in terms of production, stability and formulation of the drug as a medicine as well as ease of regulation.

2.1.4 NEW ANTIMICROBIALS

ANTIMICROBIAL RESISTANCE

According to official figures, around 25,000 people in the European Union and 63,000 people in the United States die each year from infections caused by multi-drug resistant bacteria. Furthermore, resistance to some anti-viral agents and more recently some anti-fungal medicines is starting to appear. Consequently the world urgently requires new, innovative ways of treating microbial infections to combat the significant and increasing resistance to currently available antimicrobial medicines, particularly antibiotics, as well as ensuring that currently available antimicrobials are used more effectively.⁴² In the case of antimicrobial resistance, some infections can now only be treated with antibiotics that have not been in use for decades, e.g. fosfomycin is now used for the treatment of urinary tract infections caused by extended spectrum beta-lactamase (ESBL) producing *Escherichia coli* to avoid the need for intravenous antibiotics and the hospital admission that would entail. These facts were acknowledged in a recent report by the Chief Medical Officer, Department of Health (DH) for England, which made a number of recommendations aimed at addressing the problems of antimicrobial resistance, improving hygiene, preserving the effectiveness of existing antibiotics as well as stimulating the production of new antibiotics.⁴³

LACK OF NEW ANTIMICROBIALS

Despite the well-known problems of increasing bacterial resistance, only two new classes of antibiotics have been brought to the market in the past 30 years. Very few pharmaceutical companies are currently developing antimicrobial drugs, as they are regarded as having a poorer return on investment because they are taken for a short period of time and are usually curative. This, together with the current regulatory barriers to medicines development, has led to the virtual collapse of antimicrobial research and development by the pharmaceutical industry.⁴²

Furthermore, antibiotics are known to disrupt the intestinal microbiome (i.e. 'good' bacteria present in the gut). This can lead to infections such as *Clostridium difficile* infection (CDI), which is often but not exclusively acquired in hospitals. The use of certain classes of antibiotics is causally linked to CDI, so as a consequence national policy has been to avoid these. This has meant that new antibiotics are not used in CDI, but are instead reserved for situations where no alternatives can be used in order to prevent resistance developing.

PARTNERSHIPS TO DEVELOP NEW ANTIMICROBIALS

One possible solution to encourage the development of new antimicrobials is better alignment of economic and regulatory approaches, including public-private partnerships. One such scheme is the Innovative Medicines Initiative (IMI), which is Europe's largest public-private partnership. The IMI aims to improve the drug development process by supporting the more efficient discovery and development of better and safer medicines for patients. At the end of 2011, an IMI project was launched with the aim of encouraging pharmaceutical companies to share information that could prove useful in developing new antimicrobials. This project is the first step in a wider initiative that European authorities hope will drive the development of a new generation of antimicrobials. More such initiatives are urgently needed to ensure the development of effective and safe antimicrobials. In addition, new regulatory approaches are required. For example, in the United States a new approach where the rapid approval of new antimicrobials based upon small, relatively inexpensive clinical superiority trials, particularly for serious infections caused by highly resistant pathogens, has been proposed.⁴²

2.1.5 NEGLECTED DISEASES

RARE DISEASES AND ORPHAN DRUGS

For very similar commercial reasons as for the lack of new antimicrobials, problems also exist with the availability of children's medicines, orphan drugs for diseases affecting small numbers of patients, ultra-orphan drugs for very rare diseases, drugs for neglected (developing world) diseases and pandemic flu. Indeed, it might be anticipated that a similar situation will occur when stratified medicine becomes more widely available, particularly as some groups of patients will be identified as being too small in number to warrant developing new medicines.

NOVEL APPROACHES TO DEVELOPING ANTIMICROBIALS

Plants, animals and even microbes are all being investigated as potential sources of new classes of antimicrobials.^{44,45} The marine environment, which accounts for around half of all global biodiversity, holds enormous potential for the discovery of new antimicrobial agents, as well as compounds which may improve the efficacy of current antimicrobials against resistant organisms. An alternative approach would be to develop treatments that attack microbial targets but have a reduced potential to drive resistance, such as the use of bacteriophages (viruses that infect and kill bacteria but not human cells), antivirulence drugs and immune-based therapies including infusions of monoclonal antibodies or white cells. Furthermore, the development of novel gene-specific antisense antibiotics that could be used to silence virulent or resistant genes would be useful in the future battle against drug-resistant bacterial infections.

CHALLENGE

13. Develop new antimicrobials and new approaches to treating antimicrobial infection

Initiatives that can address these commercial hurdles are urgently required to ensure the development of medicines for neglected diseases.

CHALLENGE

14. Encourage initiatives to develop new medicines for the treatment of neglected diseases, including identifying new funding streams to promote not-for-profit medicines research in neglected diseases

DEVELOPMENT OF AN ORALLY ACTIVE TREATMENT FOR THALASSAEMIA

Thalassaemia is the most prevalent inherited single-gene disorder in the world and life-saving therapy for this disease involves a combination of blood transfusion and iron chelation. Bob Hider, Prof. of Medicinal Chemistry at King's College London, is a pharmaceutical scientist who is well known for his work in haematology. Prof. Hider designed the first orally active iron chelator, deferiprone (tradenames include Ferriprox). Prior to this orally active treatment, thalassaemia was treated using desferrioxamine, an iron chelating drug administered by continuous infusion over periods of 6-8 hours. Although

deferiprone received approval from the EMA in 1999, it was not until 2011 that the FDA granted accelerated approval for the use of deferiprone in the USA. This decision – brought about largely as the result of extensive lobbying by patients – was made on the grounds that deferiprone satisfies an unmet need for a choice of iron chelation therapy for those patients in whom blood transfusion leads to potentially fatal cardiac iron burden. Deferiprone is increasingly being adopted by clinicians for the treatment of iron overload associated with the treatment of thalassaemia and sickle cell anaemia.

2.1.6 'NEW LIFE' FOR OLD DRUGS

REPURPOSING

Although not a new concept, the emergence of genomic data and a greater understanding of disease through systems biology has resurrected the idea that old drugs may find 'new life' by repositioning or 'repurposing' – a process based on the fact that drugs often interact with multiple targets and therefore in more than one disease, producing effects that can be good or bad. Repurposing is likely to increase as our understanding of pharmacogenomics expands. Repurposing an existing drug can save years of time and an estimated 40% of the current costs of bringing a drug to market by eliminating the need for additional toxicological and pharmacokinetic assessments and avoiding reformulation. The question is how best to uncover promising new indication for drugs in a systematic manner.

Drugs for which completely new indications have been found include thalidomide, withdrawn from the market in 1961 after causing thousands of severe birth defects but approved in 1998 for leprosy and in 2006 for multiple myeloma. The use of thalidomide within the NHS is now subject to strict governance and patient consent is required before treatment commences. Thalidomide is probably the first example of two chiral forms of a drug having very different pharmacological and toxicological properties. In the case of thalidomide only one of the optical isomers was genotoxic; the other isomer exhibited no toxicity. It is now commonplace to ensure that the most appropriate chiral form of a drug is used in a medicine. Sildenafil citrate, originally developed to treat pulmonary arterial hypertension, was ultimately marketed for erectile dysfunction, although it is now also licensed to treat pulmonary arterial hypertension. Other drugs are currently undergoing clinical trials for repurposing and it is likely that more existing medicines will find new indications by repurposing in the coming years.

DRUG RESCUE

A related process is 'drug rescue' where drugs that were abandoned before they could be approved by the regulatory agencies are screened to see if they can treat diseases other than those for which they were originally developed.

Both drug repurposing and drug rescue could provide a fertile source of medicines for new indications in the coming years.

CHALLENGE

15. *Encourage initiatives that support the repositioning and repurposing of drugs, where possible, for patient benefit*

2.2 Drug Formulation and Delivery

Once a potential drug or biologic has been identified, it must be formulated into a medicine before it can be

administered to humans, initially in clinical trials and ultimately in routine treatment.

2.2.1 BIOPHARMACEUTICS AND DRUG FORMULATION

BIOPHARMACEUTICS

Biopharmaceutics is the study of the relationship between the physicochemical properties of a drug (established during pre-formulation studies), its dosage form (tablet, capsule, etc) and the onset and duration of its therapeutic activity in the patient. An understanding of biopharmaceutics is a crucial part of the medicines development process and is necessary to select the type of formulation required to give the desired activity profile of the drug. For example, if a drug is intended to treat the acute pain associated with a headache, then a dosage form giving a quick release of drug, and therefore quick onset of action, is required. If, on the other hand, a drug is to be used to relieve chronic pain such as encountered in arthritis, then rapid drug release from the formulation and onset of action is not necessary and consequently a modified release formulation giving prolonged drug release may be preferable. If required, it is possible to develop formulations that give the desired drug release through incorporation in a modified release preparation.

MODELLING *IN VIVO* DRUG BEHAVIOUR

In order to speed up the formulation of a new medicine, research is needed into improved methods to more accurately relate the results obtained from *in silico* and/or *in vitro* drug release (dissolution) studies to what happens when the medicine is used in patients (*in vivo*). Advanced models of the gastrointestinal dissolution process, which include peristalsis to ensure mixing, appropriate transit times, flow of saliva, gastric and pancreatic juices including digestive enzymes and bile, are now available. At present, however, they only allow an estimate to be made of the amount of drug available for absorption rather than being able to predict how much drug is absorbed. Consequently, models that include an absorptive process which more accurately model drug behaviour in the body would be very valuable.

CHALLENGE

16. *Improve the formulation and delivery of drugs and the development of more reliable predictive and modelling methods to optimise formulations*

2.2.2 LOW MOLECULAR WEIGHT DRUGS ('SMALL MOLECULES')

SMALL MOLECULES AND THE ORAL ROUTE

Whenever a new low molecular weight drug is identified, the oral route is the preferred route of administration, with an estimated 95% of all medicines being given orally. In fact, tablets account for approximately 50% of the dosage forms on the market, with capsules being the next most common formulation. The popularity of the tablet is due to a number of factors, including the relative ease and low cost of tablet production, the high level of patient acceptability and the stability of the formulation (and of the drug contained therein). In addition, suitably formulated tablets offer the ability to alter the rate of drug release from the tablet using either dispersible or coated tablets, respectively to speed up or slow down drug release and absorption. Indeed, whenever a new drug is being formulated as a medicine, it will be formulated as an oral dosage form unless there is a good reason not to, such as the enzymatic degradation of the drug in the small intestine.

PHYSICOCHEMICAL PROPERTIES AND THEIR INFLUENCE ON FORMULATION

In order to determine whether it is possible to successfully formulate a drug as a medicine, it is essential to determine the drug's basic physicochemical properties,

including its water solubility, its partitioning between oil and water and its behaviour in different pH environments. If a drug molecule has poor water solubility, low transfer rates across the gastrointestinal membrane, or poor stability due to the low pH encountered in the upper part of the gastrointestinal tract and/or the presence of enzymes, formulation as an oral medicine becomes complex. Additionally, if the dose of drug required is very high, there may be problems making a dosage form small enough for a patient to swallow. Alternatively, if the dose is very small, problems of dose reproducibility and content may be encountered.

Increasingly, the physical attributes of active pharmaceutical ingredients and excipients are being determined to ensure that their behaviour in blending, granulating and tableting processes are consistent to ensure the quality of the final product. The use of new spectral imaging techniques has allowed the direct measurement of intact tablets to give information on percentage composition, particle size and shape, and the homogeneity of tablet constituents to be used to monitor processes and identify the causes of poor manufacturing control.

FORMULATION OF ANTI-CANCER THERAPIES

Chemotherapy is a mainstay of cancer treatment and the only therapeutic option for the treatment of disseminated disease. Led by the revolution in tumour biology, new drugs and new methods of administration of these drugs are currently being researched. Most of the new drugs considered are poorly water soluble and unstable, and so their translation into clinical therapies is critically dependent upon the

application of pharmaceutical formulation skills combined with biopharmaceutical knowledge. Pharmacist Prof. Gavin Halbert has been performing this translational role for 25 years at the Cancer Research UK Formulation Unit, achieving multiple successes (including temozolomide and abiraterone) and clinical leads for future research in areas such as targeted therapies and polymer therapeutics.

PHYSICOCHEMICAL PROPERTIES AND DRUG FAILURE

One of the reasons why drugs fail at the formulation stage of the medicines development process is the disconnect between the physicochemical properties of the molecules discovered in the hit-to-lead optimisation programmes and the properties required for the drug to become a successful medicine. In particular, there is often a lack of appreciation that a molecule will not become a successful medicine if it is not adequately distributed within the body. A successful drug requires a balance to be struck between potency/selectivity and its pharmacokinetic properties. The focus of the hit-to-lead optimisation programmes is to drive for potency at the *in vitro* level, which often translates into increased lipophilicity.

To achieve successful delivery and therefore optimal exposure of the drug to the body, however, requires an appropriate balance of oil and water solubility. Closer interdisciplinary working is helping to overcome this dichotomy, but further progress is needed to produce more 'drug-like' lead compounds by first intent, which can, at least partially, be addressed by greater involvement of pharmaceutical formulation scientists from the outset of the drug discovery process.

The involvement of pharmaceutical formulation scientists in the early stages of the drug discovery process is particularly beneficial, as their knowledge greatly aids in the selection of molecules with the most appropriate properties for successful formulation being taken forward for development as medicines, thereby helping to reduce attrition rates at a later stage in the process.

It should be acknowledged, however, that it is not always possible to select drugs with the optimal properties for formulation as a medicine. Consequently, benefit would be gained from the development of cost-effective technology platforms to overcome the problems encountered with many low molecular weight drugs, in particular molecules that have low water solubility and/or poor permeability. Over the years, many ways to resolve this problem have been proposed, although most technologies work for only a relatively limited number of molecules. The search therefore goes on for technologies to overcome the solubility/permeability problems encountered with the formulation of drugs as medicines.

NON-ORAL ROUTES OF DRUG ADMINISTRATION

If all the skills of a pharmaceutical scientist fail to prepare a suitable oral formulation, then an alternative route of administration may be sought, which often requires a more complex formulation. There are, however, cost implications associated with different (non-oral) routes of administration which may limit their use. For example, if a drug is intended for the treatment of a simple headache, then the expense associated with the preparation of an injection would not be justified. In order to formulate a drug for delivery other than by the oral route, significant advantage needs to be demonstrated over the oral route of administration or else the drug needs to be the first in its class.

There are instances, however, where non-oral routes of delivery have been successfully exploited with many playing vital roles in patient treatment. For example, transdermal delivery has been very effectively used to deliver a range of drugs with properties which prevent effective oral administration, including poor intestinal enzyme stability. Similarly, inhaled medicines play an essential role in treating asthmatic patients, significantly lowering the dose of drug needed to treat a patient by directly administering the drug to its intended site of action in the lungs. Furthermore, formulation as a liposomal injection has been employed to alter a drug's distribution and pharmacokinetic profile (and thereby therapeutic index) within the body. Parenteral formulations are frequently much more challenging formulations, not least because of the restricted range of excipients that can be used.

Indeed, although many exciting possibilities for improving the formulation and delivery of a drug have been proposed, most are far too complex and/or expensive to currently find widespread application in practice.

Consequently, research effort needs to be focused on inexpensive, practical solutions to improving drug delivery and reducing the dose of drug required, while at the same time reducing side effects.

CHALLENGE

- 17. Improve the formulation and delivery of small molecule drugs through developing and implementing simple and commercially viable technologies*

2.2.3 BIOLOGICS

PROPERTIES OF BIOLOGICS

As a consequence of the increasing use of biologics as therapeutic agents, there is an urgent need to better understand their behaviour. This includes how to characterise biologic molecules to understand their pharmacokinetics and chemical and physical stability to enable their formulation as medicines. Unfortunately, many biologics exhibit extremely poor stability and, because they are too large to be absorbed from the intestine, cannot be administered orally. Consequently, they provide significant formulation challenges and often require intravenous or other methods of parenteral administration. Furthermore, biologics tend to be far more sensitive than conventional low molecular weight drugs to the presence of additives (or excipients) such as simple buffer salts. Indeed some biologics are even sensitive to the method of dilution prior to administration. In addition, there are a number of logistical issues associated with the supply of biologics, not least being the need to ensure the integrity of a 'cold chain' as many are degraded when not refrigerated.

Monoclonal antibodies are a particular success story in the use of biologics as therapeutic agents. However, considerable effort was necessary to bring these biologics to the clinic, such as production optimisation, and further work is still required to develop safer, cheaper and more efficient therapeutic monoclonal antibodies.

NUCLEIC ACIDS IN GENE THERAPY

The formulation of nucleic acids such as DNA and siRNA as medicines for gene delivery to correct or eliminate the expression of a pathogenic protein has attracted considerable interest. This is primarily because there is potential to cure genetically-based diseases rather than alleviating symptoms, as is currently the case with many existing therapies.

Two main types of vehicle (known as vectors) are being explored for gene delivery, namely the viral and the non-viral (chemical) vector. Although viral vectors are especially effective gene delivery vehicles, there are a number of concerns around their use, including their propensity to elicit an immune response, a reduced efficacy upon repeat administration and a capacity to carry only low molecular weight DNA. Non-viral vectors offer an alternative approach and are particularly advantageous in terms of their lower immunogenicity, greater safety and greater packaging capacity.

DELIVERING GENE THERAPY TO TARGET CELLS

While it is perfectly possible to achieve gene delivery in the laboratory, the successful formulation and delivery to the target cells *in vivo* (and in the case of DNA, its translocation across the cell to the nucleus) continues to represent a significant challenge. Most gene delivery formulations will need to be delivered parenterally (in most cases via injection) although pulmonary delivery might be possible in some instances. Furthermore, it is likely that these treatments will be expensive, at least in the foreseeable future, and as a consequence limited to the treatment of life threatening and/or severely debilitating diseases. Despite the first commercialised (viral-based) gene therapy treatments being marketed in China for the treatment of head and neck cancers, and in Europe for patients with a rare metabolic disorder known as lipoprotein lipase deficiency, the promise of gene-based medicine remains largely unrealised.

IMPROVING THE IMMUNE RESPONSE TO VACCINES

Although vaccines have been used for many years, the search continues for new and improved vaccines. For example, much recent research has focused on the potential of using muramyl dipeptide, liposomes and immunostimulating complexes (ISCOMs) as adjuvants (or additives) to improve the patient's immune response upon vaccination. Alternative approaches include improving the efficiency of vaccine delivery using human and non-human adenoviruses as viral delivery vectors. DNA vaccines, which involve the injection of genetically engineered DNA to produce an immunological response, are still at the experimental stage, but have been investigated in a number of viral, bacterial, parasitic and cancer models and offer great potential.

DEVELOPING STABLE VACCINES FOR NON-INVASIVE ADMINISTRATION

Only a few vaccines, such as the polio vaccine, can be given orally. Vaccines are typically administered by injection with all the potential problems this can cause. Work is therefore underway to find alternative, non-invasive methods of vaccine delivery. Topical administration through the use of microneedles (i.e. small patches consisting of thousands of small (micro-) needles that pierce only the upper layer of the skin), and mucosal delivery, show considerable promise. Another problem

encountered with vaccines is their instability and requisite transportation and storage at refrigerated temperatures. Failures in the 'cold chain' from manufacture to administration result in the loss of nearly half of all global vaccines, while the 'cold chain' itself accounts for as much as 80% of the price of vaccinations. The development of temperature 'stabilised' vaccine products that do not require a 'cold chain' are urgently required to make vaccine distribution simpler, thus saving billions each year and offering the possibility of reaching remote areas in developing countries. The 'holy grail' of vaccine

formulation, therefore, is the preparation of a non-parenteral, i.e. oral or transdermal, vaccine which produces a high immune response but does not require cold storage.

CHALLENGES

18. *Optimise the formulation, delivery and manufacture of biologics to make products affordable*
19. *Improve the stability of and optimise the immune response to vaccines*

2.2.4 NANOMEDICINES

DEFINING A NANOMEDICINE

One area of formulation currently attracting considerable attention is the area of nanomedicine. Although considerable debate has focused on defining a nanomedicine, the MHRA has recently proposed that the term nanomedicine should be reserved for a medicine containing particles (known as nanoparticles) of which 50% are less than 100 nm in size. This definition, however, is itself open to interpretation as the measured size depends upon the polydispersity of the particles present and the technique used to measure them.

USES AND TOXICITY

While the term nanomedicine (or nanopharmaceutical) is relatively new, probably being coined in 1999, nanomedicines in their broadest sense have, in fact, been widely and very successfully used in medicine for many years. Colloidal delivery systems, such as drug-containing micelle and vesicle formulations, are examples of nanomedicines, as are biologics such as monoclonal antibodies.

Pharmaceutical scientists are currently exploring a range of very small nanoparticles of less than a few nanometers in size, which have not yet been tested in humans. These nanoparticles, which include chemically modified carbon nanotubes (hollow nanotubes of carbon) and quantum dots (such as those prepared from the semi-conducting material, cadmium selenide), are being investigated for a whole variety of purposes, including delivering light-activated drug therapies and as carrying agents in sensitive diagnostic tests. (There is currently public concern over the use of 'nanoparticles', which are reported in the press to be toxic. To date, surprisingly little research has explored nanoparticle toxicity, although much work is now underway.)

CHALLENGE

20. *Exploit the properties of nanomaterials to develop safe, advanced medicines*

2.2.5 NEW AND ENABLING TECHNOLOGIES

EXCIPIENTS IN MEDICINES FORMULATION

The pharmaceutical scientist is always searching for new and safe materials that can be used to improve the formulation of a medicine. These are known as excipients. The vast majority of those in current use were developed primarily for use by the food industry and then adopted for use in pharmaceutical products. It would be particularly beneficial to be able to design materials with the desired properties for medicines formulation, for example carrier systems for inhaled molecules. The cost of developing a new material/excipient designed specifically for use in medicines is, however, very high as any new material, even if that material is intended to be inert, must be subject to expensive toxicity studies to ensure its safety. New excipient development is an area where pharmaceutical companies could greatly benefit from working together to reduce development costs.

DELIVERY AND SAFETY OF MEDICINES

One area which is potentially a source of innovative technologies that can be used to deliver both drugs and biologics is the interface between pharmaceutical sciences and engineering. A number of successes have been achieved in this arena. These include child-resistant containers to reduce the likelihood of children getting access to a medicine, tamper-evident packaging to indicate if adulteration has occurred and blister packaging

for increased medicines stability. In addition, syringe drivers have been revolutionary in allowing patient-controlled analgesia, while auto-injectors, which are used to deliver adrenaline intramuscularly, have saved the lives of many patients who have had acute anaphylactic reactions. Metered dose inhalers and dry powder inhalers are in routine use for respiratory conditions.

NOVEL METHODS OF DELIVERING DRUGS

The transdermal patch is an excellent example of an innovative technology where engineering was applied to the biological sciences to achieve a desirable outcome. The success of the transdermal patch is based on it being a non-invasive means of delivering potent drugs over a prolonged period of time, while overcoming important problems such as short biological half-lives of elimination, inconvenient dosing regimens, adverse events associated with overdosing/underdosing and/or large first-pass effect, and potentially toxic metabolites. More recently, microneedles are an excellent example of the pharmaceutical and (bio)engineering sciences coming together to produce a painless, practical and economically viable method of effectively delivering drugs into the skin, which should find wide exploitation in the future.

MICRONEEDLES

Novel drug delivery systems can enhance the clinical benefits of existing drugs and meet the challenge of delivering the new drugs of the future. Pharmaceutical scientists have a well-established track record in designing and developing innovative drug delivery systems that provide real benefits for patients. This is exemplified by the work of pharmacist Prof. Ryan Donnelly who is developing microneedles, arrays of tiny needles that painlessly, and without drawing blood, pierce the skin to facilitate delivery of vaccines, peptide and protein drugs and allow

minimally invasive patient monitoring. The possibilities for microneedle-enhanced patient care are wide ranging. For example, those in the developing world are set to benefit from cheaper vaccination and premature babies from blood-free sampling of drug substances and biomarkers. Prof. Donnelly has received considerable recognition for his work, being the recipient of several prestigious awards, including the Royal Pharmaceutical Society's 2011 Science Award, the 2012 GSK Emerging Scientist Award and the BBSRC Innovator of the Year Award in 2013.

DEVELOPING NOVEL DEVICES

It should be realised, however, that for every innovative device that succeeds, many more potentially valuable ones fail for a variety of reasons. These reasons include expense but more often because pharmaceutical companies focus predominantly on the development of the medication, rather than the device needed to deliver the drug. As a result, the device design is overlooked until late in the development process when it is too late to change the medicine. Consequently, there is a need for device manufacturers to work alongside the pharmaceutical formulation scientists in the pharmaceutical industry at an early stage in the medicines development process to ensure the production of novel, cost-effective delivery devices that meet the needs of the population at which they are targeted. For example, a large inhaler device that does not allow the easy and discrete administration of a dose of drug would not be popular with patients.

DEVELOPING 'SMART' MEDICINES

To date, it has not been possible to develop a truly 'smart' medicine that does not just deliver a drug but delivers it in the amount and rate required by the body at the right time and in the right place. In order to achieve this goal, some feedback mechanism is required. Indeed, a means of achieving feedback-control is another of the 'holy grails'

of drug therapy, and while experimental systems have been developed that show potential, for example in the treatment of diabetes, none are commercially available for use in a patient-friendly, minimally invasive fashion.

A theranostic combines a diagnostic and a drug/biologic into a single device or system, and may provide a means to achieve feedback-control. A biologic (e.g. insulin) and diagnostic (blood glucose monitoring) could both be present on a small chip that can be placed inside a diabetic patient. When the chip records a rise in blood glucose levels it can stimulate the release of the required amount of insulin to reverse this rise. Progress in microfluidics, microfabrication and miniaturisation in general, coupled with novel, ultra-sensitive biosensors for drugs, or endogenous biomarkers, are currently opening the way to link a diagnostic device with a drug delivery platform to create a 'smart' medicine. Some 'smart' medicines have already undergone trials in humans, although it will be some time before simple and easy-to-use devices become available for use in the wider patient population.

CHALLENGES

21. *Work to improve the range of excipients available for use in pharmaceutical formulations*
22. *Develop and implement new and innovative technologies for the delivery of small molecule drugs and biologics, which may incorporate feedback-control*

2.3 Stratified Medicines

It has long been known that there is a huge variation in the way individuals respond to and handle drugs. The first observations of genetic variation in drug response date from the 1950s when it was observed that the muscle relaxant suxamethonium chloride and drugs such as isoniazid were metabolised by the enzyme N-acetyltransferase at different rates depending upon what form of the enzyme the person possessed. A more recent example are many psychoactive drugs which are now known to exhibit genetic-based interpatient variability.⁴⁶

ROLE OF PHARMACOGENETICS AND PHARMACOGENOMICS IN PATIENT STRATIFICATION

Since the first observations, pharmacogenetics and pharmacogenomics have evolved into scientific disciplines in their own right, offering the very real opportunity of personalising medicines for the individual, with drug choices, doses and administration regimens being tailored specifically to the pharmacogenetic profile of the patient. While it is not usually possible to individually tailor (or personalise) a medicine to a specific patient, it is becoming a realistic proposition to stratify (or group) patients to allow for targeting of treatments to the sub-population of patients who will respond to the treatment, thereby allowing preventative or therapeutic interventions to be concentrated on those who will benefit.

Although not a new concept, stratified medicine has only become a realistic proposition for the treatment of many diseases because of the recent advances made in pharmacogenetics and pharmacogenomics.

GENETIC VARIATION AND DRUG RESPONSE

Alongside this improved understanding of the genetics of disease, is the increasing realisation that in diseases such as type 2 diabetes and asthma, environmental and lifestyle factors, such as diet and smoking, can also play a significant part. It is widely recognised that not all drugs work for all patients with the disease (i.e. a 'one size fits all' approach does not always work). Indeed, it has been reported that, depending upon the disease and the underlying genetics, only between 20-75% of patients respond to a class of drug.⁴⁷ For example, due to genetic variation in the gene that codes a receptor on the surface of the smooth muscle cells lining the airways of the lungs, some patients do not respond to the bronchodilator salbutamol. Furthermore, it has recently been found that the use of salbutamol in patients with a specific gene variant can result in exacerbation of their symptoms, thus illustrating the importance of understanding the role of genetics in the treatment of disease.

For stratified medicine to become a reality, however, a significant number of scientific, ethical and social barriers need to be overcome, as well as a consideration of the likely cost and whether it is feasible for all patients to access stratified medicines for their particular medical condition(s).

GENETIC TESTING AND GENE DELIVERY

Genetic testing can be used to identify changes in chromosomes, genes or proteins that can be linked to specific conditions, including cystic fibrosis, haemophilia A and thalassaemia. Indeed, the first genetic test on humans was performed in 1934. The potential to replace a faulty gene, express a therapeutic protein or halt the expression of a faulty protein offers promising strategies for developing a cure (as opposed to a treatment) of genetic and acquired diseases and is the concept behind gene delivery. While it is possible in the laboratory to achieve gene delivery, this research is still at a relatively early stage, with much work remaining to create therapies that are safe and effective for long-term use and are accessible to whole patient populations.

USE OF BIOMARKERS IN STRATIFIED MEDICINE

Biomarkers are becoming an increasingly important tool in stratified medicine. A biomarker is any biological molecule, including a gene, protein, receptor, enzyme or metabolite, that can be used to indicate whether an observed physiological message is normal or abnormal. For example, biomarkers can be used diagnostically to identify gene mutations that put patients at risk of developing future disease. The expression of the BRAC1 and BRAC2 genes as an indicator of the likelihood of a woman developing breast cancer is probably the best known example. Biomarkers can determine a patient's suitability for a specific drug treatment, such as establishing the appropriate dose of a medicine or determining HER2 status in breast cancer to indicate whether treatment with trastuzumab (better known by its trade name, Herceptin) is likely to be effective. Indeed, medicines intended to treat cancer are increasingly being launched with a so-called 'companion diagnostic' – a test allowing doctors to determine whether the patient has the right genetic make-up to respond to treatment, thereby improving efficacy and safety, and making drugs more cost-effective. Currently, there are around a dozen drugs in Europe that have companion diagnostics, although it is not always a regulatory requirement that such a test is used. More recently, biomarkers can also indicate whether a patient might be at risk of developing adverse events, e.g. the use of HLA (human leucocyte antigen) testing to reduce the risk of severe skin reactions associated with the medicine abacavir used to treat the HIV infection.

DIAGNOSTIC TESTS TO IDENTIFY PATIENTS AT RISK OF DEVELOPING A DISEASE

It is imperative that cheaper diagnostic tests are developed to identify patients most at risk of developing specific conditions. Ethical questions continue, however, about the use of genetic tests to identify a patient who is currently asymptomatic but shown to be at risk of developing a disease, particularly where no treatment currently exists. It is essential that there is a concomitant drive to develop and approve the treatments for such conditions. The fact that many biomarkers can be detected using non-invasive techniques involving saliva, urine, sputum and exhaled breath offers the exciting potential for the pharmacist to become more involved in the near patient testing, diagnosis and, for some diseases, prescribing.

Counselling of patients by pharmacists must be an integral part of such a role. Such activities will build on current pharmacy involvement in diagnostic testing and monitoring of patients.

POLYGENIC DISEASE AND EPIGENETICS

While stratified medicine presents huge opportunities for the future, it is not without significant challenges. The genetic causes of disease are often complex, with only a very small number of conditions existing where a single genetic defect is responsible for the disease (i.e. the disease is monogenic). In the vast majority of cases, multiple genes that interact with each other are involved (i.e. the disease is polygenic), and two individuals will rarely have the same combination of defective genes. The position is further complicated by the fact that epigenetics, including environmental and lifestyle factors such as diet, may contribute to the progression of a disease, or the response to a medicine, in ways that are not detected through genetic profiling. This will make treatment with stratified medicines much more difficult and complex and will require a range of different stratified medicines to treat all forms of a disease.

REDESIGNING CLINICAL TRIALS

The development of a stratified medicine will present significant challenges for clinical trials designs. Patients will be selected on the basis of their genetic composition. Smaller numbers of patients may be required in clinical trials and more defined end points will be necessary, although this may not necessarily make trials any less expensive to carry out due to the increased extent of testing of patients and tissues.

PAYING FOR STRATIFIED MEDICINES

As well as the scientific challenges posed by stratified medicine, there will also be considerable economic challenges. There are significant costs involved in the development of a stratified medicine as it will be necessary to produce smaller batches of a medicine and/or an increased number of variants. Such investment costs will have to be recovered from a much smaller potential patient population. Although the initial cost of providing a stratified medicine to a patient may be high, the ongoing healthcare costs to the NHS associated with this patient are expected to be less and may consequently predicate a new model for reimbursement of drug costs. In addition to the scientific and economic challenges, there are also a number of ethical, legal and social issues that all need to be fully considered.⁴⁸

TAILORING MEDICINES TO AN INDIVIDUAL PATIENT'S REQUIREMENTS

While there is much interest in stratified medicines based on a patient's genetic make-up, tailoring a medicine to the specific needs of a patient is not a new concept and is something that has been practised in some form for decades. Patients often have the dose of their medicine based on their own individual factors such as body weight, body surface area, renal function or hepatic function. Such tailoring has often involved the preparation of a specific product for a patient, often by a 'specials' manufacturer, and there may be a future role for increased customisation of medicines at the point of use.

DIAGNOSTIC TESTS FOR CURRENT MEDICINES

If suitable diagnostic tests were to be developed for medicines that are currently available, there could be an appropriate selection of patients for whom the medicine is more suitable. At present, however, there is greater emphasis within the pharmaceutical industry to develop a diagnostic test for a new medicine than to investigate the pharmacogenetics and to develop a diagnostic test for a currently marketed product. Partnerships between the pharmaceutical industry, the diagnostic industry, the NHS and also charities may be one route to initiate such a development and thereby improve the use of currently available medicines. One positive development in this area is that while the cost of sequencing the human genome for the first time was just less than \$3 billion, the cost of determining the complete genome of an individual, has progressively come down and is now just over £1,000.

USE OF STRATIFIED MEDICINES

The potential of stratified medicine to improve the efficacy of a drug at the same time as reducing adverse events is extremely exciting, but many hurdles must be overcome if the potential of stratified medicine is to be realised. As new medicines become more focused in the patient population they treat, it is important that economic models are developed that provide appropriate incentives for developing drugs with small target populations, as well as developing mechanisms that allow equitable access for all patients to stratified therapies. Building on the rapidly expanding pharmaceutical science knowledge, economic incentives, regulation and integration into education will all influence the rate and extent to which stratified medicine becomes integrated into drug development and clinical practice, and delivers on the promise of new and specific therapies for patients.

CHALLENGES

23. *Educate the public and patients about the ethical and moral issues surrounding the use of new technologies*
24. *Expand the concept of personalising medicines for all patients*
25. *Improve targeting of medicines to specific populations through the use of biomarkers with the aim of reducing attrition rates during medicines development*
26. *Develop models that encourage innovation in stratified medicines, which embrace economic, regulatory and ethical issues and make cost-effective treatment available to patients*

2.4 Pharmacokinetics and Pharmacodynamics

Once a potential drug candidate has been identified, its fate and behaviour in the body have to be assessed before a decision can be made whether it is possible to develop the molecule into a safe, effective medicine. In particular, the drug's physicochemical, pharmacokinetic, pharmacodynamic and toxicological properties all have to be established. The primary goals of clinical pharmacokinetics include enhancing efficacy and decreasing toxicity of a patient's drug therapy. Indeed, UK pharmaceutical scientists have been at the forefront of the development and application of physiologically based pharmacokinetic and pharmacodynamic (PBPK-PD) modelling.

As a consequence, this has resulted in considerable advances being made in the ability to predict the effects of demographics, race, age, genetics, formulation, disease, pregnancy and drug-drug interactions on drug exposure. The concept of PBPK-PD modelling is to 'learn' about the system and its important covariates and to design and power appropriate clinical studies to 'confirm' the predictions. This approach is proving to be particularly valuable for recommending dosage in neonates/children and pregnant women, where real studies are difficult to do, not least for ethical reasons.

DRUG MONITORING AND TITRATION

For some medicines, the development of strong correlations between serum concentrations of medicines and their pharmacologic responses has enabled clinicians to apply pharmacokinetic principles to actual patient situations. Currently, about 30 drugs, including warfarin, are therapeutically monitored as the concentration range in which they exert their therapeutic effect without eliciting significant side effects is small. Pharmacists use the results from therapeutic drug monitoring to ensure the dose administered is achieving the required blood levels in the patient and recommend changes to the dose where necessary. Where such correlations do not exist, the dose of a medicine administered to a patient may be titrated to obtain the desired clinical effect.

FACTORS AFFECTING PHARMACOKINETICS AND PHARMACODYNAMICS

As a consequence of differences due to age, gender, weight and the genetic make-up of the patient, a drug might not exhibit the same pharmacokinetic and pharmacodynamic behaviour in all patient groups. In addition, underlying medical conditions, pregnancy, concurrent medicines use as well as the environment and lifestyle choices (smoking, alcohol consumption and obesity) can all impact on the way in which a particular patient responds to a medicine.

EFFECTS OF AGE (SEE ALSO SECTION 3.3.3 SPECIAL PATIENT GROUPS)

Specific patient groups including younger and older people, those who are critically ill and those who have an end stage organ failure (e.g. liver or kidney) require special consideration. This is due to differing physiological, pathological and developmental characteristics, which are known to significantly impact on the pharmacokinetics and pharmacodynamics of a medicine. Despite this awareness, there is limited pharmacokinetic and pharmacodynamic information for these patient groups;

this means that recommended doses of drugs in such individuals may be based on inaccurate information rather than robust scientific evidence. It is clear that a defined process urgently needs to be developed, starting with clinical trials in specific patient groups and ending with policy and practice initiatives, which recognise the complexity of medicines use in such populations.

CHALLENGE

27. *Promote clinical trials in specific populations to ensure the dose is right for the patient*

TAILORING THE DOSE OF A MEDICINE FOR A CHILD

Children are not small adults, and it is essential to understand that children's bodies respond to medicines in a different way than adults. Children need medicines that are tailored to their age, body weight and physiological condition. Until recently, only three broad age bands were used to define how much oral liquid paracetamol should be given to children between the ages

of 3 months and 12 years. In 2011, the Medicines and Healthcare Products Regulatory Agency (MHRA) issued new dosage guidance that increased the number of age bands to 7, with a single dose per age band making it easier for parents and carers to know exactly how much paracetamol they should give their children.

2.4.1 THE YOUNGER POPULATION (SEE ALSO SECTION 3.3.3.1)

EFFECT OF CHILD DEVELOPMENT ON DRUG HANDLING

In terms of healthcare, children are defined as the group from birth to 16 or 18 years of age. It is well established, however, that major physiological changes, including different rates of maturation in systems affecting drug handling, occur between birth and the late teenage years.⁴⁹ Most of the systems involved in the absorption, distribution, metabolism and excretion of drugs have reached maturity by about 3 years of age. As a consequence, children under the age of 3 are most at risk. For example, child development rates mean that the intramuscular route in the infant is unreliable due to poor muscle blood flow,⁵⁰ while the extent of drug absorption via the transdermal route is often greater with subsequent risks of toxicity, especially in premature neonates. The blood-brain barrier is another system that is widely considered to be immature in the very young

with the result that a greater distribution of drugs into the central nervous system can occur, leading to toxicity. Furthermore, the volume of distribution of many drugs is increased in neonates, infants and children due to a reduced plasma protein binding and a greater extracellular fluid volume as a proportion of total body water. These changes can result in an increased elimination half-life for certain drugs.

METABOLIC HANDLING AND RENAL EXCRETION

Some drug metabolic processes are immature at birth, leading to reduced drug clearance and prolonged elimination half-life, and there may be reduced pre-systemic (first pass) metabolism, resulting in greater bioavailability. Renal excretion in the newborn is reduced but reaches levels approaching the adult state after around a year. All of these differences mean that it is not correct to simply assume that children, and in particular

very young children, are small adults for which the adult dose of a drug can simply be scaled down proportionately. While it may be possible to allometrically scale the dose for body size for older children, this is not possible for very young children. Consequently, in order to ensure the optimal use of medicines, more research is required to understand the pharmacokinetics of drugs, particularly in the very young. As very little is known about how maturation influences pharmacodynamics, further research is required in this area.

SUITABLE DOSAGE FORMS

Coupled with a lack of understanding of a child's pharmacokinetics and pharmacodynamics is a paucity of information about the best dosage forms to administer to a child and how they should be formulated. Rather than administer a conventional solid dosage form typically used in adults, it is common practice to use alternative formulations such as oral liquid dosage forms for a child as it is easier to administer an oral liquid to a young child. Similarly, when a parenteral route of delivery is necessary, the less invasive methods such as topical delivery or rectal administration are more acceptable than injection. Many of the medicines used for children are, however, not licensed for use in this patient group and it has been estimated that less than 50% of medicines used for children in the European Union have been studied in this population.⁵¹ As a consequence, practitioners may be in a position of prescribing a formulation which is of unknown efficacy in children.

FORMULATING MEDICINES

Wherever feasible, formulations as free as possible of excipients should be developed and used in children. Indeed, formulating for the younger population can present a considerable challenge, especially when developing oral liquids because of the requirement to ensure their palatability without compromising bioavailability, the chemical/physical stability of the medicine and their preservation when multiple dose containers are necessary. Many of the excipients used in preparing medicines have not been specifically tested in children for toxicity. If they are to continue to be used in the future, particularly in neonates and infants, their safety profiles need to be established. For example, ethanol is the second most common excipient after water in liquid formulation yet little is known about the effects of ethanol in children and especially in infants, neonates and premature neonates. Benzyl alcohol, another

commonly used excipient, can cause fatal toxic syndrome in low birth weight neonates with large quantities of propylene glycol are associated with adverse effects on the central nervous system of neonates and children.

CLINICAL TRIALS IN THE YOUNGER POPULATION

Children have been described as 'therapeutic orphans' due to the lack of commercially available, age-appropriate licenced medicines. This is often because of the lack of clinical trials involving children. One of the arguments put forward for excluding children from clinical trials relates to the ethics of involving children in trials. This must be balanced, however, by the ethical concerns about administering a medicine to a population in which the medicine has not been tested. Following the lead taken by the United States, the European Union now has regulations requiring pharmaceutical companies to study new or adapted medicines in children if there is likely to be therapeutic benefit. To encourage pharmaceutical companies to make the required investment in research into children's medicines, incentives such as an extension to patent protection or periods of product exclusivity have been introduced.

In spite of these regulatory developments, it is still the case that many medicines, both old and new, have not been fully tested in children and are often used 'off-label'. As a consequence, it is imperative that when children use medicines observational studies are conducted. This will improve knowledge of effective dose, possible side effects and reduce future inappropriate use. In the UK, Medicines for Children Research Networks have been established by the Department of Health to facilitate both industry-sponsored and academic research in this area. In order to optimise the use of medicines in children, it is essential that these networks continue to receive appropriate levels of support.

AREAS FOR RESEARCH

There is a need to continue the research and development of less invasive and less demanding clinical trial methodologies such as pharmacokinetic/ pharmacodynamic modelling, population pharmacokinetics and sparse data analysis, generalisability, microdosing, microassay and less invasive methods of monitoring.

2.4.2 THE OLDER POPULATION (SEE ALSO SECTION 3.3.3.2)

THE AGEING POPULATION

Older (or elderly) people have been traditionally defined as those over the age of 65, but to consider those over the age of 65 as a homogeneous group is too simplistic. Improved lifestyle and diet means that our older population is, in fact, more likely to be fitter and more active than in previous generations, and to live longer. This fact, coupled with the low birth rate in the UK, is resulting in a change in the demographic profile, causing an increasing proportion of older people in the population. One consequence of the increase in life expectancy is the relatively rapid rise in the prevalence of diseases of old age, such as Alzheimer's disease for which there are at present few treatments. As the population ages, it will therefore become increasingly important that clinically effective and cost-effective medicines that meet the needs of older people are available.

IMPACT OF CHANGES IN PHARMACOKINETICS ON DRUG HANDLING

Changes in the pharmacokinetics and pharmacodynamics of drugs in older people (and particularly in those who are frail) are known to influence the effectiveness and toxicity of medicines. It is known that, in older people, drug absorption alters due to changes in gastrointestinal blood flow and motility, and there is reduced liver clearance of drugs mainly due to reduced blood flow and shrinkage in liver mass. Renal function declines with ageing due to changes in the kidney and a reduced muscle mass. Changes in the pharmacodynamics of the cardiovascular system and nervous system are also well documented. All these changes associated with ageing mean that typical 'adult' doses, dosage forms and dosing regimens may not be appropriate for the older population. Compounded with this is the fact that inter-individual variability in physiological responses increases with age. The presence of co-morbidities and polypharmacy further complicates the situation. The resulting situation must be carefully managed to maximise the benefits of medicines, while at the same time reducing adverse events, in a population with an increased likelihood of contraindications and potential for drug interactions.

CLINICAL TRIALS IN THE OLDER POPULATION

Older people have been traditionally ignored and excluded from clinical trials, largely because they often have several other pre-existing medical conditions. This is despite the fact that they are active consumers of medicines and have much to gain from such trials. Conducting trials in older patients has the distinct advantage of replicating the true clinical situation by observing the possible benefits and risks of medicines in patients with co-morbidities and on polypharmacy regimens, i.e. the typical patient.

Clinical trials in the older population are now being actively encouraged by regulatory agencies. Conducting clinical trials in older age groups is not without its challenges: appropriate and relevant outcome measures must be identified. Surrogate outcomes may not be relevant to the older population. Furthermore, it should also be recognised that due to co-morbidities, medication problems, such as drug interactions, are much more likely to be missed in the older population and as a consequence the performance of clinical trials on such patients could also have significant benefits in terms of optimising medicines use.

CHALLENGES

28. *Develop age-appropriate dosages and formulations based on pharmacokinetic, pharmacodynamic and pharmacogenomic information*
29. *Develop patient-centred medicines, including combination formulations*

3. BETTER USE OF MEDICINES

3.1 Introduction

All pharmacists delivering front line care to patients and interacting with professional colleagues draw constantly on their core skills and knowledge of fundamental pharmaceutical science and the available evidence. These skills and knowledge are used when making the professional and clinical judgements that support the optimal prescribing, supply and use of medicines. Pharmacists working in these clinical roles will also supplement their core pharmaceutical science knowledge with additional skills and knowledge required to perform their more specialist roles.

PLACE OF RESEARCH

Ideally, all pharmacy activities should be supported by high quality research, which draws often on the theoretical frameworks and research methodologies of the social and behavioural sciences. Other factors, however, drive pharmacy policy, and decisions are sometimes made in the absence of good research evidence, with data being gathered and reviewed after implementation.⁵³ Whilst accepting that clinical pharmacy practice is sometimes driven by policy without underpinning research, the objective of this following section is to highlight areas where practice has been informed by research and to suggest areas where further research is required.

CHALLENGE

30. Increase the research capacity and capability within the profession

SERVICES DELIVERED BY PHARMACY

Community pharmacy is the window into the NHS on every high street and has been promoted as the first port of call for promotion of health and well-being, prevention of ill health, treatment and advice on minor ailments, management of long-term conditions, and support and advice on medicines. The network of community pharmacies is highly accessible to patients and the public, with 99% of the population able to access a pharmacy within 20 minutes by car and 96% by walking or using public transport.⁵⁴ The location of community pharmacies,

particularly those in more deprived communities, offers opportunities to reduce health inequalities, whilst the long opening hours of many pharmacies make them readily accessible to patients.

As well as being trusted by patients and the public, community pharmacies provide an obvious location for delivery of NHS primary care and public health services. Over 85% of pharmacies now have consultation areas where they can undertake confidential discussions with patients. Some pharmacies also carry out testing for diabetes, high blood pressure, cholesterol and *Helicobacter pylori* (for peptic ulcer disease), monitoring patients with chronic obstructive pulmonary disease, and assessing the International Normalized Ratio (INR) of patients taking warfarin.

The accessibility and informality of pharmacy encourage patients to feel comfortable in raising difficult or embarrassing health issues. It also means that when patients present with one problem, pharmacists can opportunistically broach broader issues of general health, targeted to that patient. Lifestyle is increasingly recognised as being a causal factor in the aetiology of major morbidities and pharmacists can play a central role in influencing behaviour change. Those pharmacists working more closely with the primary healthcare team within GP practices can improve the safe and effective use of medicines and provide targeted additional support to those in greatest need, improving the overall efficiency of GP-based primary care services.

Traditionally, pharmacists have been integral to the detection of prescribing errors before they reach the patient. Medicines reconciliation on admission to, and discharge from, hospital expands this traditional role and is recognised as a key factor in reducing prescribing errors.⁵⁵ Most UK acute care hospitals provide a clinical pharmacy service to the majority of in-patients, as well as selected outpatients, and this includes as a minimum, daily prescription review, medicines reconciliation and support in discharge planning. Within a London Trust that consists of three hospitals with 1,100 beds, more than 2,000 clinical pharmacy interventions (optimising medicines use,

detection and prevention of prescribing errors pharmacist consultations) are made every week; on average, per 100 bed days, 47 interventions were made by pharmacists to patient care.⁵⁶ Since the pharmacist's clinical role was first developed in the hospital sector over 30 years ago, the role has greatly expanded and ranges from pharmacists preparing total parenteral nutrition solutions to

prescribing medicines for highly complex patients, such as those in critical care. Furthermore, it is now commonplace that other healthcare professionals refer patients to a pharmacist if there are complex and challenging medicines issues to resolve. For the contemporary hospital pharmacist, pharmaceutical science pervades every aspect of their role.

GUIDELINES TO INCREASING DRUG EFFICACY

Obesity rates in the UK are the third highest in Europe and have increased dramatically over the past few years.⁵⁷ Obesity is fast becoming a major burden on the NHS. The management of infections in obese patients is problematic due to an increased risk of morbidity and mortality as well as a lack of information about dosing information. Pharmacists play an increasingly important role in the management of obese patients undergoing antimicrobial therapy because of the patients' altered pharmacokinetic handling of drugs. Optimising the efficacy and minimising the toxicity of antibiotics in this patient group requires a level of understanding of pharmacokinetic and pharmacodynamic principles that is uniquely provided by pharmacists.

To date, only a few antibiotics, such as aminoglycosides, vancomycin, daptomycin and linezolid, have been sufficiently well studied in the obese population to allow recommendations to be made on altered dose. For some antibiotics, such as gentamicin and vancomycin, the use of ideal body weight or adjusted body weight rather than actual body weight is recommended, while for other antibiotics, including penicillins, cephalosporins, meropenem and aztreonam, a dose at the upper end of the recommended dosage range is proposed.⁵⁸ Pharmacists have been instrumental in developing local guidelines to enable safer and more efficacious prescribing of these classes of drugs.

3.2 Optimising Medicines Use and Decision Making

Medicines account for over 12% of the total yearly NHS budget (about £123 billion across Britain in 2011/2012), generally increasing yearly beyond the rate of inflation. Of the total primary care budget, about a quarter is due to prescription medicines.⁵⁹ There is a constant tension between containing this medicines budget at affordable levels, whilst at the same time making new, effective (and often more expensive) therapies available to patients.

Ensuring medicines are used appropriately so that patients get safe, clinically and cost effective care is a fundamental role for pharmacists today, whether working in strategic or patient-facing roles. Using their expert knowledge of pharmacology and therapeutics, they are well placed to ensure optimal outcomes from medicines.

This role was first envisaged by Hepler and Strand in 1990 and defined as 'the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life'.⁶⁰ The authors also noted that 'pharmaceutical care is provided for the direct benefit of the patient and the pharmacist is responsible directly to the patient for the quality of care'. Since that time, the term pharmaceutical care has become understood internationally as the aspirational role for pharmacists. The extent that it has been implemented varies geographically but the UK has been at the forefront. In Scotland, the term pharmaceutical care remains current. Pharmaceutical care, defined as the responsible

provision of drug therapy to achieve agreed outcomes that improve an individual's quality of life, is a core component of the most recent pharmacy strategy.⁶¹ It involves co-operation with the patient, and if appropriate their carer and other professionals, in designing, implementing and monitoring a pharmaceutical care plan that will produce a specific therapeutic outcome for the patient.

The term medicines optimisation has recently been introduced in England to describe the process of ensuring the safe and effective use of medicines and to enable the best possible outcomes for patients.⁶²

3.2.1 CLINICAL ROLES FOR PHARMACISTS

Clinical pharmacy has been defined by the American College of Clinical Pharmacy as a health science discipline in which pharmacists provide patient care that optimises medication therapy and promotes health, wellness and disease prevention with the practice of clinical pharmacy embracing the philosophy of pharmaceutical care.⁶³ Clinical pharmacy involves assessing the patient to inform choice of medicine, ongoing monitoring of the effects and side effects of the medicine and making dose adjustments as needed within agreed parameters.

Clinical pharmacists are regarded as the experts in therapeutic use of medicines. They provide patient care

that optimises the use of medicines for patients in all settings, often collaborating with medical and other healthcare professionals.⁶¹ The clinical roles of pharmacists result in benefits to patients, for example, through reducing medication errors and involvement in medicines reconciliation.⁶⁴⁻⁶⁷ A recent research study involving 17 intensive care units demonstrated that over half of the pharmacist interventions related to optimising the use of medicines.⁶⁸

Pharmacists working in hospital, primary care and community pharmacy, as well as those working in commissioning and medicines management, are all

SHARED RECORD KEEPING AMONG HEALTHCARE PROFESSIONALS

Pharmacists often get requests for medicines out of GP hours when it is not possible to get access to the patient information that they need to help ensure they supply the right medicine. Pharmacists' access to patient records is pivotal to reducing medication errors, improving medicines adherence and ensuring the provision of safe and more effective care to patients. The Scotland Patients Association recognises that increased roles for pharmacists within hospitals, primary care and the community should be an asset to patients and other health professionals, provided there is improved continuity of care for

the patient and excellent communication between all health professionals. To achieve this will require accurate records to be kept and shared amongst health professionals, whilst maintaining patient confidentiality, and patients must be able to check their records for accuracy. In order to feel safe and confident, patients need to trust health professionals and sufficient time must be allotted to explain any new treatments or medication to patients. Pharmacists' access to a patient's medical record is crucial to improve patient safety through knowledge of an accurate patient diagnosis and all prescribed medicines.

in ideal positions to influence both the prescriber and the patient and thereby ensure optimal medicines use. In addition, pharmacists themselves may now be prescribers. By having access to patient records, pharmacists would be able to further improve clinical interventions, prescribing and patient safety. Being able to articulate the pharmacist's contribution to patient care and public health is becoming increasingly important in all areas of healthcare.

3.2.1.1 Developing Guidelines

THE SCOTTISH MEDICINES CONSORTIUM

The purpose of the Scottish Medicines Consortium is to assess the evidence for clinical effectiveness and cost-effectiveness of newly licensed medicines, and to accept into routine use as quickly as possible those medicines that provide good value for money to NHS Scotland so that patients can benefit. To do this, the Consortium analyses information supplied by the drug manufacturer on the health benefits of the drug and the justification of its price. The Consortium is made up of clinicians, pharmacists and health economists together with representatives of health boards, the pharmaceutical industry and the public. The past chair of the Consortium is pharmacist Professor Angela Timoney, Director of Pharmacy at NHS Lothian. Pharmacists on the Consortium use their knowledge of pharmacoepidemiology, pharmacoconomics, public health, the critical appraisal of evidence and a statistical oversight, together with an awareness of the science behind systematic reviews and meta-analyses, to assess information supplied by medicines manufacturers on the health benefits provided by medicines and whether this justifies the associated cost.

Pharmacists have contributed in many ways to improving the clinical and cost-effective use of medicines by applying their pharmaceutical science knowledge of therapeutics, pharmacoepidemiology and health economics. Utilising their understanding of the science involved in the critical appraisal of the available evidence, and the underpinning scientific philosophy behind evidence-based medicine, pharmacists contribute to the post regulatory evaluation of the clinical and cost-effectiveness of medicine.

One example of this would be contributing to health technology assessments (HTA) that may be undertaken by the National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG).

Pharmacists also contribute to other national bodies to develop practice guidance on the use of medicines, following the best available evidence' e.g. SIGN (Scottish Intercollegiate Guideline Network). The advice from these bodies is implemented locally, for example by Drug and Therapeutics committees, and pharmacists are core members of these. Thus the best use of public monies by the NHS is assured. Pharmacists also use their clinical knowledge, and their skills in collating and assessing the available evidence, to contribute to Cochrane Reviews, which are internationally recognised systematic reviews of health issues. Increasingly, the pharmacist's beneficial contribution is being recognised by Governments across the UK.

3.2.1.2 Medication Review (see also section 3.3.3.2)

Medication review encompasses a spectrum ranging from a full clinical review of a patient's medicines to a more general medicine use review⁶⁹ and evolved from clinical hospital pharmacy practice. Early research conducted in the mid 1990s demonstrated that a hospital clinical pharmacist, based in a general medical practice, could improve the cost-effective and clinically effective use of medicines in patients such as those on peptic ulcer therapies.^{70,71} This was the basis on which practice pharmacy evolved and practice pharmacists now routinely advise GPs and patients about medicines. Community pharmacists have also taken on a medication review role, originally as part of small feasibility studies or research projects.⁷²⁻⁷⁴ Evidence has shown that when pharmacists advise prescribers about individual therapies, such as

NHS NEW MEDICINE SERVICE

The NHS New Medicine Service (NMS) in England, which started October 2011, is targeted to patients with long-term conditions that have been prescribed new medicines. It is anticipated that the NMS will lead to a variety of beneficial outcomes, including improved medicines adherence, reduced medicines wastage and an increased patient engagement with their condition and medicines, which will help them make decisions about their treatment and self-management. The NMS resulted directly from research on medicines adherence carried out by pharmacist Professor Nicholas Barber, Director of Research, The Health Foundation (formerly Professor of the Practice of Pharmacy, University College London). Indeed, much of Prof. Barber's research has focused on understanding what is currently wrong with things in order to establish how to do things better, then to introduce and evaluate services which should achieve this end. For example,

Prof. Barber has evaluated electronic prescribing in primary care, automated dispensing systems, the prevalence and causes of prescribing errors in general practice, the implementation of the national Care Record Service in England and medication errors in nursing homes. The findings of these studies in medicines safety and behavioural medicine have influenced UK pharmacy practice and policy. In 2013, Prof. Barber and Dr Hamish Wilson published a 'Review of NHS Pharmaceutical Care of Patients in the Community in Scotland', a document that informed the Scottish Government's 'Prescription for Excellence: A Vision and Action Plan for the Right Pharmaceutical Care through Integrated Partnerships and Innovation'. Prof. Barber's work has been recognised in the award of the Guild of Healthcare Pharmacists' Gold Medal and a lifetime achievement award by the Royal Pharmaceutical Society.

the management of hypertension, they can make recommendations for changes to a patient's medication regimen, so that patients have better clinical outcomes; for example, more people attain their target blood pressure when compared with usual care.⁷⁵ More recently, the role has been delivered through locally commissioned schemes, and ultimately nationally through the NHS community pharmacy contractual frameworks (Medicines Use Reviews and New Medicine Service schemes in England, Discharge Medication Review Service in Wales and Chronic Medication Service in Scotland). Crucially, this role would be even more effective if pharmacists had access to a patient's medication record.

3.2.1.3 Prescribing

Non-medical prescribing, which includes pharmacist prescribing, has more recently further increased the potential for pharmacists to implement medication

changes and is gradually being introduced in primary and secondary care. The number of pharmacist prescribers is, however, relatively small, and those involved are the early adopters. Prescribing competences are, however, increasingly being embedded in the undergraduate pharmacy curriculum and consequently, in the future, graduates will have the qualifications to prescribe. Research shows that whilst generally well received, organisational barriers often delay implementation of pharmacist prescribing.⁷⁶ Research also suggests that patient outcomes are improved when a long-term condition, such as chronic pain, is managed by pharmacist prescribers.⁷⁷ It is recognised in general that small trials often show benefits that are not sustainable when larger numbers are involved. The challenge remains to deliver the benefits of pharmacy prescribing when the service is rolled out to the whole pharmacy population, as well as ensuring that the skills of all pharmacist prescribers are fully utilised.

CHALLENGES

31. *Develop effective methods for assessing patients' medicines needs to improve the safe, effective and efficient use of medicines, thereby optimising their use*
32. *Increase the involvement of pharmacy in prescribing and review of medicines use, including more roles for the pharmacist as an independent prescriber*

3.2.1.4 Self-care and Over-the-Counter Medicines

SUPPORTING PATIENTS

A core role of community pharmacists and their associated staff has always been to support patients in managing their health by supplying over-the-counter (OTC) medicines and/or advice. This role has always been widely recognised as a useful adjunct to the NHS, providing quick and convenient access to advice and treatment for conditions not requiring a medical consultation. Research has shown that patients prefer to use their pharmacist for advice on the management of minor illness, rather than any other professional.⁷⁸ Through the concerted efforts of the profession and the pharmaceutical industry, the role has been enhanced by a steady stream of reclassifications from prescription-only status to pharmacy supply. In addition, a selection of these medicines has been made available to those members of the public less able to afford them through minor ailment services⁷⁹ in England⁸⁰ and Scotland.⁸¹ Whilst the rate of reclassification has decreased recently, key products continue to be switched. It is important, however, that the extensive training and knowledge of pharmacists is recognised and considered when reclassifying medicines and that effective doses of OTC medicines are made available for sale.

CLINICAL EFFECTIVENESS OF OTC PRODUCTS

Prior to reclassification of some medicines from prescription-only medicines (POM) to pharmacy medicines (P), minimal evidence existed of the clinical effectiveness of OTC products. Medicines which have undergone reclassification, however, are more likely to be supported by evidence of their effectiveness (see below) and, in some cases, also their cost-effectiveness.^{82,83}

Nicotine replacement therapy⁸⁴, anti-fungal agents for the management of vaginal candidiasis⁸⁵ and orlistat to assist weight loss in obese patients⁸⁶ are a few examples of OTC medicines, which are supported by strong evidence from randomised controlled trials and meta-analyses. Similarly,

more robust evidence now exists regarding the lack of clinical effectiveness as well as potential harm associated with other OTC medicines, e.g. some cough preparations,⁸⁷ which has also informed practice through the issue of restrictions regarding their use.

ACCESSING EVIDENCE

The availability of evidence alone is not sufficient to change a pharmacist's practice nor a patient's knowledge and demand for these medicines. Pharmacists and their staff need to be able to access information rapidly and with ease in order for it to have utility during consultations with their patients. Familiarisation with, and use of, sources of information would assist pharmacists and their teams in keeping up to date with new evidence to inform their recommendations and practice. The aim of this is to develop a condition-based approach rather than a product-based approach. The involvement of pharmacy teams in the development of evidence-based portfolios for the use of OTC medicines has been explored and early results are promising.⁸⁸ New approaches to the collation and promotion of this evidence are needed to enhance practice and ultimately improve patient care.

PATIENT CONSULTATIONS

Not only do pharmacists and pharmacy personnel need to access evidence from existing sources, they also need to seek relevant information from patients or customers during their consultations for OTC medicines in order to determine the most appropriate course of action. Evidence-based outcomes are more likely to be achieved as more information is exchanged.⁸⁹ It is not only the obtaining of information that is important, however, but also the individual staff member's ability to use this information to influence the consultation outcome.⁹⁰ Enhancing the communication skills of pharmacists and their staff will contribute to the evidence-based supply of OTC medicines and advice.⁹¹ In addition, pharmacists should be proactive in recording self-care interventions and it should be part of pharmacy culture to take part in post-authorisation studies after reclassification.

CHALLENGES

33. *Establish an evidence-based approach to all OTC advice and medicines supply*
34. *Improve communication skills of pharmacists and their staff*
35. *Introduce a culture of intervention recording and involvement in post-authorisation studies of OTC medicines*

3.3 Medicines Use

3.3.1 CONSEQUENCES OF INAPPROPRIATE MEDICINES USE

Considerable resources are devoted to developing new and improved medicines and getting them to market. If patients do not take their medicines appropriately, however, then they will fail to achieve the intended health benefits and all the effort of developing medicines is wasted. On average, 50% of patients taking medicines for chronic conditions do not take them as directed, however this can be increased dramatically with pharmacist interventions leading to avoidable ill health and economic loss to the healthcare system and society in general. Research has shown that 6% of UK hospital admissions are related to adverse drug reactions, equating to 4% of hospital bed capacity.^{11, 92, 93} Furthermore, patient adherence to medicine-taking regimens, i.e. the extent to which a patient's medicine taking matches what has been agreed between them and the prescriber, is recognised as a global issue, as evidenced by a World Health Organisation report in 2003.⁹⁴

3.3.1.1 Concordance

The context of whether patients take their medicines or not has been transformed over recent years. Initially, there was simply the move from using the term 'compliance' to 'adherence' – the difference being that the latter referred to taking medicines according to an agreed plan between the patient and professional. The move to using the term 'concordance', however, was of a much bigger scale.⁹⁵ A patient cannot be 'non-concordant' in the way that they can be described as non-adherent. Only a relationship (i.e. that between the patient and the professional) can be concordant or not. In the concordance model of medicine taking – often now referred to as 'partnership in medicine taking' – patients are regarded as equals in the consultation and in decision-making.⁹⁶

3.3.1.2 Adherence Issues

IMPACT OF NON-ADHERENCE

Much has been learnt in recent years about the nature of non-adherence to medicines. It is now recognised that non-adherence should not be viewed as a problem of a particular type of patient, but rather a problem that is complex, involving both behavioural and practical aspects, and one that is likely to affect many patients at some time. Adherence to some medicines such as oral anticoagulants, anticonvulsants or antituberculosis therapies is particularly important as missing only a few doses can have clinical consequences in terms of disease control. In the control of HIV infection, the target for adherence is 95% or greater as adherence below this level is associated with an increase in the patient's viral load,⁹⁷ similarly poor adherence with antibiotics can result in increased bacterial resistance.

INTENTIONAL AND UNINTENTIONAL NON-ADHERENCE

In any attempt to improve adherence, it is critical to differentiate between intentional non-adherence (related to a patient's beliefs about a medicine) and unintentional non-adherence (due to barriers that may stop a patient taking a medicine as intended) as this will be crucial to the development of solutions. It is known that intentional and unintentional non-adherence are common, and for any approach to be successful all healthcare professionals involved must realise and accept that patient involvement may mean that the patient decides not to take (or to stop taking) a medicine.⁹⁸

The periodic review of a patient's medication is essential, as issues relating to both intentional and unintentional non-adherence are likely to change over time. As the most accessible healthcare professional, the pharmacist is in the ideal position to monitor adherence and to identify patients who are experiencing difficulties taking their medicines as agreed. Any interventions that contribute to improved patient adherence to their medicines regimen, such as the New Medicine Service and Medicine Use Reviews in England and the Chronic Medication Service in Scotland, will not only provide better clinical outcomes for the patient, but also reduce medicines wastage.

EFFECTS OF NON-COMPLIANCE

It is estimated that between 30-50% of patients who are prescribed medicines for chronic conditions do not take them as directed; this results in avoidable ill health and considerable economic loss to the healthcare system and indeed to society in general. Rob Horne, Prof of Behavioural Medicine, School of Pharmacy, University of London addressed this problem through a phased approach to developing effective interventions to non-adherence. Working with health psychologists, Prof. Horne developed a range of tools and models for assessing patient perspectives of illness and treatment, e.g. the Beliefs about Medicines Questionnaire (BMQ) and the Medication

Adherence Report Scale (MARS), as well as frameworks (a Necessity-Concerns Framework) for understanding treatment-related behaviours with a particular focus on adherence to medication. This work translates into a portfolio of theory-based pragmatic interventions to help patients get the best from treatments by supporting optimal adherence and self-management. These tools balance the concerns people might have about the disadvantages of medicine taking against their beliefs in the medicine's effectiveness and contribute to the understanding of why medicines may or may not be taken by patients.⁹⁹

INTERVENTIONS TO IMPROVE ADHERENCE

NICE, in its clinical guideline on medicines adherence,¹⁰⁰ found only limited evidence that interventions work to improve patient adherence. Indeed, it is acknowledged that it is unlikely that a single intervention, or a single consultation style adopted by a healthcare professional, will suit all patient groups; support for an acute condition is likely to require a different approach to long-term treatment for a chronic condition. Partnership in medicines taking, i.e. allowing the patients full involvement in decisions about medicines, is one of the focuses of this NICE guideline. Similarly, a Cochrane review⁹² found that simple interventions could be useful in increasing adherence and improving patient outcomes for short-term treatments. For long-term conditions, however, no simple intervention, and only some complex ones, produced improved health outcomes for patients. Adherence issues of particular relevance to young people are referred to in section 3.3.3.1.

Pharmacists currently use a number of strategies to assist patients in improving their medicines adherence, with the use of a telephone intervention from a pharmacist having been shown to improve adherence in some patients newly prescribed a medicine.⁷² Sophisticated methods aimed at monitoring patient adherence have also been investigated. One recent development involves patients

swallowing a microchip, which can gather information about medication taking to help identify adherence issues and also provide information on the patient's body temperature and heart rate by sending signals to a smart phone. These microchips have been approved for use as medical devices in Europe and in the United States.

Although there are relatively few studies demonstrating that pharmacist interventions are successful in supporting adherence, there are examples of pharmacist interventions helping improve adherence to immunosuppressive medication in renal transplant patients, antihypertensive medications and asthma products. Such information on pharmacist interventions is critical for pharmacy if it is to demonstrate its added value in the supply and use of medicines. To support patients to take their medicines effectively will require a consultation and prescribing process that allows and encourages patient input and involvement, a well-informed patient with access to information which meets their medicine information needs, and an effective method of 'pharmaceutical needs assessment' and 'medication review'. This process must involve all relevant health professionals, including pharmacists, but with the patient at the centre.

CHALLENGES

36. *Develop strategies and research evidence to improve patient adherence to medicines*

37. *Facilitate partnerships between the patient, their carers (where appropriate) and the multidisciplinary team in medicines taking*

3.3.2 PATIENT INFORMATION

DESCRIBING RISKS AND BENEFITS OF MEDICINES

In order for partnership in medicine taking to become a reality, information that reflects the more detailed and scientific-based information contained in the Summary of Product Characteristics aimed at healthcare professionals must be made available to patients to support their decision-making. In particular, there is a need for patients to be adequately informed of the benefits and risks of taking any medicines. To convey information about the risks and benefits to patients during consultations or to the public about screening or public health initiatives, healthcare professionals must be able to understand, report and communicate statistics around risks and benefits.

It has been shown that the best way to describe how often side effects to medicines occur is to use natural frequencies (e.g. affects 1 in 100 people),¹⁰¹ although the number needed to harm (NNH) (e.g. NNH 132, meaning 1 patient will be harmed out of 132) has also been suggested. In terms of describing the benefits of treatment, while the best way of achieving this is not yet known, the number needed to treat (NNT) has been proposed.¹⁰¹ Initial research suggests that giving people numerical information about the likelihood of benefit in this way may result in the public expecting a higher likelihood of benefit than is actually the case – especially for preventative medicines.¹⁰²

PRESENTATION OF INFORMATION

Patients require information to help them make a decision about whether to start taking medicine and also with ongoing decisions in managing their medicines. They will obtain information from spoken, written and web-based sources. Most of the spoken information gained by patients comes from an interaction with a healthcare professional and although spoken information continues to be a very important form of communication for many patients, it is well established that most spoken information is rapidly forgotten.

Although written material is useful as an information source after spoken information has been given, patients do not want written information to substitute for

spoken information. Patients value written material as a useful source of information but only to support the spoken information. Studies have shown that people have concerns about the complex language and poor visual presentation of written information about medicines, and that they value written information that is tailored to their individual circumstances and illness.¹⁰³

The challenge of information provision to patients by healthcare professionals is to develop a process that provides sufficient clearly presented, plain language information in a range of formats, which meets an individual patient's needs in terms of their illness and circumstances. In addition, the information obtained from different sources must be consistent, so that the same message is given to patients irrespective of whether this is obtained from spoken, written or reliable internet sources.

PATIENT INFORMATION LEAFLETS AND USER TESTS

Patient information leaflets are required by European law to be included with all medicines and are a source of reliable information for patients, which reflects the more detailed and scientific-based information contained in the Summary of Product Characteristics aimed at healthcare professionals. Recent European law requires pharmaceutical companies to ensure the package leaflet has been tested in the relevant patient group and is legible, clear and easy to use.¹⁰⁴ One way that this can be satisfied is by undertaking a well-designed and executed 'user test' of the patient information leaflet, although a 'user test' itself is not mandatory. This testing of patient information leaflets has increased the focus on the quality of these leaflets to ensure that the language used can be easily understood by patients.¹⁰⁵ Pharmacists have a role to play in providing a patient with any additional information they require and in discussing the issues around efficacy and the risks of side effects to ensure they have the information they need to make informed decisions about their medicines.

QUALITY OF INTERNET INFORMATION

The availability of information on the internet means that many patients have access to a wide range of information about their disease and medicines before, during and after consultations. While some of this information is excellent, other information is of much poorer quality and may be subject to commercial influence. There is a need to ensure that accurate information is available for the public and that pharmacists direct patients to reliable sources of medicines and health information.

PHARMACISTS' ROLES IN PROVIDING INFORMATION

With an increasingly well-informed public comes a greater expectation of health knowledge amongst pharmacy practitioners. Pharmacists in professional and clinical practice must contribute to, and use, information systems to offer personalised healthcare to patients. Increasingly, community pharmacy will become the principal focus for evidence-based medicines information, lifestyle diagnosis and advice on therapeutic options. Technological advances are driving the development and application of health-monitoring technologies. The increasing availability of testing kits and monitoring devices is also more widespread and can feedback monitoring information to pharmacists and other healthcare professionals. This places more emphasis on disease prevention and lifestyle management, with patients increasingly being expected to take responsibility for their own health and well-being.

CHALLENGE

38. *Provide patients with accessible and readable information, which describes the chance of benefit and the risk of harm, allowing them to make informed decisions about whether a medicine is right for them*

3.3.2.1 Health Literacy

IMPACT OF LOW HEALTH LITERACY LEVELS

Health literacy is an important aspect of patient adherence. Health literacy encompasses not only people's ability to read and understand health information, but also their wider ability to engage with the healthcare process, including the use of medicines. Research has shown that between a third and a half of people in developed countries have difficulty understanding and engaging with the healthcare process, and that this is associated with poorer health outcomes and increased mortality.¹⁰⁶

Low health literacy levels have also been recognised as an area of concern in patient safety and adherence to treatments. A prime example relates to many patients' inability to use devices such as inhalers, with pharmacists ideally placed to help such patients. Improving health literacy is an essential part of enabling the pharmaceutical needs of minority groups to be met and includes helping patients acquire the necessary knowledge and skills to understand and manage their long-term conditions, reduce their risk factors for future long-term illness and encourage effective self-care.

INCREASING HEALTH LITERACY

The goal of increasing health literacy is to improve health outcomes, but it must be recognised that patients who are informed may make decisions they consider to be right for them, but which may not be the best course in the opinion of the healthcare provider. Further research is required to evaluate attempts by healthcare professionals and health systems to improve patient understanding and engagement.

EXPERT PATIENTS

At the other end of the spectrum is the expert patient. Patients with long-term illness can develop such expertise regarding their pathology and treatment that in many cases they will know more than the healthcare professional. Pharmacists, like all the members of the multidisciplinary team, must respect these patients' knowledge and needs. Information and counselling regarding medicines use must be adapted to ensure an appropriate level of delivery.

CHALLENGE

39. *Support patients to become well informed about their medicine taking and respect the needs of the expert patient*

3.3.3 SPECIAL PATIENT GROUPS

In general, the special patient groups most frequently encountered in pharmacy, and in particular in community pharmacy, are children (and their parents) and older people. These special groups present particular challenges in terms of the selection of a suitable medicine at an appropriate dose. Children and older people are not generally included in clinical trials and there are challenges in attempting to extrapolate data generated from trials involving only the adult population. In addition, children and older people present specific challenges around adherence. Other special patient groups that are increasingly encountered in pharmacy are patients with long-term conditions such as those with mental health conditions, renal failure and HIV.

Pharmacists are ideally placed to make positive interventions at several stages of the pharmaceutical care process involving special patient groups, and the evidence base is emerging to support the role of the pharmacist in managing high risk medicines in high risk populations, such as the young and older people.

3.3.3.1 Younger Patient Groups (see also section 2.4.1)

MEDICINES IN CHILDREN

Most children are exposed to medicines from an early age as a result of acute conditions such as respiratory infections, diarrhoea and vomiting, or chronic illnesses such as asthma and allergy. They are also likely to receive immunisations from the age of a few months. For children with special or complex needs it is essential to make medicines administration as quick and easy as possible, particularly in situations where the child is responsible for taking their own medicines. Improving medicines adherence in children, particularly young children, through the use of new technologies that have particular appeal to this patient group also needs further investigation.

Medicines reconciliation in children can present significant challenges for healthcare professionals, especially when the child has complex and frequently changing medicines regimens. Pharmacists have been crucial in developing workable procedures to ensure effective medicines reconciliation when children move between healthcare settings.

MEDICINES AND YOUNG PEOPLE

Young people in the second decade of life also have challenges with medicines. At this time of rapid physical, emotional and social change, and developing capacity for independent decision-making, adherence is generally worse than in either younger children or adults.¹⁰⁷ Furthermore, taking medicines for an otherwise 'hidden' condition can make the young person view themselves as not being 'normal'.¹⁰⁸ To get the best outcomes they must engage with medicine taking but may have to manage significant side effects. Partnerships with parents around medicines taking are crucial during adolescence;¹⁰⁹ some young people manage their own medicines from an early age,¹¹⁰ but for others, responsibility must be transferred at the right pace.¹¹¹ It must also be recognised that children's parents can also influence any decisions made about a child's medicines and this can also impact on medicines adherence. Pharmacists need to explore the context of a teenager's life, their insights and experience, to agree realistic goals with them.

GUIDANCE ON SUITABLE MEDICINES FOR CHILDREN

The British National Formulary for Children (BNFC) brings together the available evidence, best practice guidelines and advice from clinical experts to support the safe and effective selection of medicines, formulations and doses in children. Guidance has also been published around the management of Total Parenteral Nutrition (TPN) in children, neonates and premature babies to improve practice and reduce the risks associated with TPN.¹¹²

NEED FOR EVIDENCE

High quality research is urgently required to determine the most appropriate and effective way to manage medicines in children. There remains a paucity of evidence and information about the use and adverse events of medicines in children or the best way to reduce medication errors. There is also little evidence to indicate which dosage forms are most suitable for children of a particular age, or how the different ways of delivering a medicine to a child can influence adherence.

RESPONSIBLE USE OF ANTIBIOTICS

It is essential that antibiotics are used responsibly, so that the right drug is provided at the right time, in the right dose and for the right duration. Too low a dose could result in killing the weaker bacteria, allowing stronger, more virulent bacteria to thrive. Although it is now widely recognised that the age-related average weight of children is much higher now than in the 1950s, the child dose of antibiotics has remained exactly the same over this period, resulting in significant under-dosing and thereby contributing to the development of antibiotic resistance. The penicillin V dosing regimens for children first appeared in 1963-1966 British National Formulary and have not been changed since, with the recommended single dose halving between successive age bands: child 12-18 years (500 mg), 6-12 years (250 mg), 1-5 years (125 mg), < 1 year (62.5 mg). In the same period, the adult dose has increased no less than four times.¹¹³

PHARMACISTS' ROLES

Pharmacists, as experts in medicines, play a vital role in multidisciplinary teams involved in providing complex treatments to children such as intravenous administration, HIV treatments and palliative care. They must ensure both successful continuity of treatment and avoidance of medication errors by establishing good communication channels with other healthcare professionals.

CHALLENGE

40. *Improve understanding of the medication and pharmaceutical care needs of children*

3.3.3.2 Older Patient Groups (see also section 2.4.2)

Medicines are an important and common healthcare intervention for older people, with the development of new medicines contributing to the decline in mortality and increased life expectancy seen in western populations in recent decades.

POLYPHARMACY

Older people often have multiple disease conditions requiring treatment with many different medicines. This is known as polypharmacy.¹¹⁴ The challenge is to deliver evidence-based approaches for each condition, whilst avoiding contraindicated medicine use and drug interactions. Polypharmacy is a major cause of hospitalisation of older patients and an unnecessary cost to the NHS. In Scotland, pharmacists have had a lead role in the development of the recently launched Polypharmacy Guidance, which summarises the evidence base and includes a set of tools to allow clinicians to implement change.¹¹⁵

MEDICINES USE IN OLDER PATIENTS

In a study of over 12,000 participants from England and Wales, 11% of people aged 65-74 and 15% of those over 75 were taking five or more medicines and that adherence to a medicines regimen decreases significantly if more than four medicines are prescribed.^{116, 117}

The incremental benefit a medicine may have when added to existing therapies is often not well understood, and evidence to indicate the impact that a medication regimen will have on a patient's quality of life is frequently lacking. In addition, prescribing too many medicines to older people can result in the development of adverse drug events.

Particular care is required to ensure adverse events to medicines are recognised and are not interpreted as a new disease requiring further treatment. This potentially spiralling sequence of events where a new medicine is added to a patient's medicine regimen to counter the side effects of a previously prescribed medicine is known as the prescribing cascade.

The use of appropriate formulations, suitable methods of administering the medicines and means of improving adherence will benefit older people. Major physiological and cognitive changes may occur in older people and these have implications for the formulation of medicines given to older people. Age-related decline in visual function may lead to difficulties in reading medication instructions, in adhering to regimens and correct use of medicines. The ability to swallow may also deteriorate with ageing, and this is particularly problematic as the oral route remains the most dominant route of administration for most formulations. This difficulty may be compounded in conditions such as Parkinson's disease, dementia and stroke.

Cognitive decline may lead to difficulties with timing of medicines and adherence with complex medication regimens or using certain types of delivery systems, e.g. inhalers and the use of some topical products. Patients with conditions such as arthritis may find it difficult to manipulate certain formulations or remove a medication from its packaging. Although child-resistant packaging may confer a degree of safety in some respects, it may also mitigate against an older person being able to remove a product from a bottle or blister pack.¹¹⁸

REVIEW OF MEDICINES

As a consequence of having multiple medical conditions, some older people frequently need help with the complex medication regimens they require to manage these conditions. The regular review of medicine regimens and goals of treatment in older people is critical to ensure optimum and appropriate treatments, but also to ensure that any medicine that no longer confers benefit is discontinued.

It has been shown that pharmacists involved in delivering pharmaceutical care to care homes and care of the elderly wards in hospitals can contribute to the appropriate use of medicines through delivery of pharmaceutical care.^{120,121} In the community, pharmacists carrying out medicines use reviews may encourage patient adherence and independent living for as long as possible. Additionally, the role of pharmacists in identifying any potential problems with high-risk medicines, such as those used in dementia, has been highlighted. Older people are also likely to be cared for by many healthcare professionals and social workers, as well as moving between different care settings, and the pharmacist can make a major contribution in ensuring a consistent and accurate medication record is available to avoid medication errors, duplication and omissions.

CHALLENGE

41. *Increase understanding of the causes of medication errors and the impact of pharmacy interventions*

MEDICINES USE IN AN OLDER POPULATION

Currently, over 10 million people in the UK are over 65; this number is expected to increase to 19 million by 2050. These numbers are already placing considerable strain on social services and on residential care and nursing homes. Carmel Hughes, Prof. of Primary Care Pharmacy, Queen's University Belfast focuses her research on the quality of drug use in older people, particularly in the long-term care setting. Her research has investigated the internal and external factors which influence prescribing, including adversarial legislation, organisational culture and multidisciplinary collaboration. This has led to the development of a unique pharmaceutical care intervention model. When tested in a cluster-randomised controlled trial, the model produced encouraging results, suggesting that the intervention was clinically effective and cost-effective. This intervention model has now been commissioned as part of a new service that will be made available to nursing homes across Northern Ireland. Prof. Hughes was the first pharmacist to be awarded a Harkness Fellowship in Health Care Policy from the Commonwealth Fund of New York City and a National Primary Care Career Scientist Award from the Research and Development Division of the Department of Health. She was awarded the 2001 British Pharmaceutical Conference Medal. She has been a Cochrane Fellow, is a member of the Cochrane Collaboration and is Joint Clinical Lead for the Northern Ireland Clinical Research Network.

3.3.3.3 Other Patient Groups

Medicines are a key intervention in many long-term conditions, including mental health, HIV medicine and renal medicine.

PATIENTS WITH MENTAL HEALTH CONDITIONS

Mental health is a diverse and challenging area of medicine. In many mental health sub-specialities, including clinical depression and schizophrenia, medicines and cognitive behavioural therapies are the most important interventions.¹²² There has been a number of new groups of medicines over the last 25 years, including selective serotonin re-uptake inhibitors (SSRIs) and atypical antipsychotics, however there has been a paucity of evidence that demonstrates these new medicines show clinical benefit over existing therapies.

Thus modern mental health is very much about medicines management: selecting the right drug for the right patient and minimising adverse effects. Pharmacists have been instrumental in guiding medication selection in mental health, with texts such as the Maudsley Prescribing Guidelines not only influencing prescribing in the UK but also being highly acclaimed internationally.¹²⁴

PATIENTS WITH HIV

In HIV medicine, antiretroviral therapy (ART) is given to reduce the mortality and morbidity associated with chronic HIV infection. The overwhelming majority of patients who receive ART experience long-term virological suppression and good treatment outcomes.¹²⁵ This compares favourably with other developed countries. Recent data have shown that the life expectancy in the UK of someone living with HIV infection has improved significantly over recent years but remains 13 years less than that of the UK population. The effectiveness and tolerability of ART has improved significantly over the last 15 years and treatment should improve the physical and thereby psychological well-being of people living with HIV infection.¹²⁶ Thus optimising the use of medicines is an essential component of modern HIV medicine and the specialist pharmacist (and in some cases pharmacy technician) is present in every HIV clinic throughout the UK.

THE MAUDSLEY PRESCRIBING GUIDELINES

Mental illness is a growing problem in all areas of the world, affecting over a billion people at some point in their lives: lifetime risk of severe mental illness (schizophrenia and bipolar affective disorder) is 2.5%; depression 20% and anxiety 20%. Drug therapy is the mainstay of treatment in all of these conditions but prescribing is complex and optimal prescribing is rarely achieved. Prof. David Taylor, Chief Pharmacist, South London and Maudsley, NHS Foundation Trust, London is lead editor of The Maudsley Prescribing Guidelines. These Guidelines which have been in continuous publication since 1994 are currently in their 11th Edition; they provide the only comprehensive evidence-based guide to psychotropic prescribing, and influence national and international prescribing. They are standard issue in the English-speaking world and have been translated into nine languages, to date selling more than 200,000 copies worldwide. Prof. Taylor's research programme provides data to support guidance within the publication. The current Guidelines include over 100 references to Prof. Taylor's work. The Guidelines represent the only comprehensive guide to evidence-based prescribing in mental illness in the world and are widely regarded as an essential text. The status of the Maudsley Prescribing Guidelines is such that other guideline bodies such as NICE make every effort to make their guidelines consistent with those in the Maudsley Guidelines.

PATIENTS WITH RENAL DISEASE

Renal medicine is highly complex and requires input from the entire multidisciplinary team. Therapy with medicines is both diverse and wide ranging, and there is a multi-faceted role for the specialist pharmacist and pharmacy technician from medicine reconciliation to supporting adherence to medicines regimens in patients on dialysis programmes. Immunosuppression therapy is a key intervention, without which there would be no

transplantation programmes. Pharmacists are involved in all aspects of therapy, from ensuring the patient gets the right immunosuppression therapy at the right time to interpretation of serum levels and dosing.¹²⁷

CHALLENGE

42. *Manage medicines appropriately to achieve optimal outcomes in vulnerable patient groups, such as young and older patients*

3.4 Public Health

Pharmaceutical scientists have for many years made important contributions to public health through the innovation of new medicines, ensuring their supply to patients in a convenient, timely manner and providing

general advice to the public. With increasing patient contact, pharmacists with clinical roles in all settings can support the delivery of key public health messages to patients.

3.4.1 PHARMACY AND PUBLIC HEALTH

While the early role for pharmacy in public health involved the supply of medicines, several of the newer extended pharmacy roles deal with provision of services. These services, however, are usually derived from a public health initiative involving medicines. Needle exchange schemes, for example, developed as a result of pharmacy involvement with drug misusers through the supply of methadone for their addiction (see 3.4.3.2 Drug Misuse). As the public health role for pharmacy continues to develop, evidence must be generated to demonstrate which pharmaceutical interventions can be most efficiently and effectively delivered.

PUBLIC HEALTH DOMAINS

The public health agenda is wide ranging in both its remit and geographical relevance. The Faculty of Public Health describes public health under the three core domains of Health Improvement, Health Protection and Improving Services, with much of the agenda being influenced by wider determinants beyond health. Through the 2 billion visits members of the public make to the 14,100 registered pharmacies in Great Britain each year, pharmacy and pharmacists, with their scientifically-based clinical education and training, are in an ideal position to support these domains. The devolved GB nations are increasingly aware that pharmacy is currently an

underutilised resource in the public health arena, and recent policy documents (e.g. Health and Social Care Bill in England, Prescription for Excellence in Scotland⁶¹) and reviews (Community Pharmacy Review in Scotland,¹²⁸ National Assembly for Wales Inquiry into Community Pharmacy 2012) underline this.

INITIATIVES TO INCREASE INVOLVEMENT OF PHARMACY

An All-Party Pharmacy Group was set up in 1999 to raise awareness of the profession of pharmacy and to promote the pharmacist's current and potential contribution to the health of the nation. A decade later, following the 2010 publication of the English White Paper 'Liberating the NHS', a Forum for Pharmacy and Public Health was established with a remit to develop standards for public health practice. In order to most effectively optimise the contribution of pharmacy and pharmacists, robust research is required to identify and deliver effective interventions. The broadening of the Faculty of Public Health beyond just those medically qualified has facilitated formal recognition of pharmacy.

ROLES FOR PHARMACY IN PUBLIC HEALTH

Pharmacy can support the public health agenda by changing attitudes and effecting culture change. It can contribute to promoting healthy lifestyle choices and to the prevention and management of infectious disease. It is imperative that the potential contribution of pharmacy as a key player be embedded in any new national or international strategy for public health.

3.4.2 HEALTH IMPROVEMENT

One of the main objectives of the health improvement agenda is to help people to live healthy lifestyles, make healthy choices and reduce health inequalities. Smoking, poor diet, which is linked to obesity, and alcohol consumption are modifiable behaviours linked to serious diseases, such as diabetes, cardiovascular disease and cancer. Without urgent action the resultant burden of disease will become unaffordable for the NHS. Pharmacists play an important role in improving public health by modifying certain lifestyle behaviours. Indeed, part of the current contract between the NHS and community pharmacy requires pharmacists to promote healthy lifestyles (England and Wales) and to provide smoking cessation and emergency hormonal contraception services (Scotland and Wales). As many community pharmacies are sited in areas with high levels of deprivation, higher than average morbidity and low levels of health literacy, pharmacists in such locations are especially well placed to have an important role in supporting the public health agenda.

The Healthy Living Pharmacy (HLP) initiative in England is a network of accredited community pharmacies. HLPs aim to improve public health at a local level, deliver high quality and consistent health and well-being advice, with the public either receiving or being signposted to services such as help to stop smoking, weight management, harm reduction and advice on alcohol consumption.

3.4.2.1 Smoking Cessation, Emergency Hormonal Contraception, Alcohol, Weight Management and Sexual Health

Evidence suggests that the health improvement role of the pharmacist could be further extended to the benefit of the health of the nation and the NHS. Strong evidence exists to support the role of the pharmacist in smoking cessation.¹²⁹ In Scotland, where smoking cessation is a national service, 70% of attempts to quit smoking come from community pharmacy schemes; in England, where it is not a national service, it is only about 20%.¹³⁰ There is also evidence to show that supply of emergency hormonal contraception services from pharmacies, whether by prescribing protocols or OTC sale, is viewed positively by both users and pharmacists and is not associated with an increase in risky behaviour.¹³¹ Evidence for other sexual health services, weight management and alcohol screening, however, is limited. Further studies need to be undertaken to confirm the value of these and support the case for changing community pharmacy contracts across all countries of Great Britain.

CHALLENGES

43. *Increase pharmacy's evidence-based contribution to health improvement, in particular in the community pharmacy setting*
44. *Reduce smoking, obesity and alcohol consumption – a challenge for all health professionals*

3.4.3 HEALTH PROTECTION

Health protection is the field of public health that is involved with the protection of the public from communicable disease. It includes areas such as infection control measures and vaccinations, as well as health screening. As the role of the pharmacist has developed, there is increasing involvement in health protection activities at the strategic level (e.g. the development of antibiotic formularies) and the individual level.

3.4.3.1 Infection control

The importance of hygienic practices must not be underestimated and pharmacists have a clear role to play in giving advice on general hygiene, wound care, and the management of spread and transmission of infection.

Pharmaceutical scientists have been active for many years in the design and development of infection control agents for disinfection and antisepsis, and more recently in advising on the effective use of new technologies for the control of healthcare associated infection (HCAI).

European policy on controlling the risk of cross-resistance from injudicious use of biocides is being influenced by UK pharmaceutical scientists.

3.4.3.2 Antibiotics

The increasing development of resistance to currently available antibiotics is a potentially serious threat to public health. There is increasing evidence demonstrating the potential harm from unnecessary use of antibiotics, such as antimicrobial resistance in an individual lasting up to a year.¹³² The appropriate prescribing of antibiotics by healthcare professionals and the proper use of prescribed antibiotics by the public is essential if the risk of further antimicrobial resistance is to be minimised. Furthermore, there must be a reduced expectation by the public of receiving an antibiotic treatment for conditions that are unlikely to be bacterial or are self-limiting.

ANTIMICROBIAL STEWARDSHIP

The profound consequences of antibiotic resistance for individual patients and for society create an ethical and moral imperative to protect public health by all reasonable means. Antibiotic stewardship has two primary goals: firstly, to optimise clinical outcomes while minimising unintended

consequences of antimicrobial use and secondly, to reduce health care costs without adversely impacting quality of care.¹³⁶ At the individual patient level, stewardship has been defined as 'the optimal selection, dosage and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance'.¹³⁷ At the organisation level, the term antibiotic stewardship refers to specific programmes and interventions to monitor and direct antimicrobial use at a healthcare institution, thus providing a standard evidence-based approach to judicious antimicrobial use.¹³⁸ Surveys of physicians report a lack of knowledge and confidence around antimicrobial stewardship.

The NHS recognises the burden, both financially and in terms of patient impact, caused by antimicrobial resistance such as methicillin-resistant *Staphylococcus aureus* (MRSA) and the growing problem of carbapenem-resistant *Enterobacteriaceae* (CRE) which are resistant to nearly all antibiotics.¹³³

Pharmacy has played a significant role locally, nationally and internationally in antimicrobial stewardship to ensure antimicrobial guidelines are evidence based, that patients are reviewed daily to stop or de-escalate to less powerful antibiotics and that regular antimicrobial audits and reviews of use are performed. Pharmacy involvement in the development of OPAT (outpatient antibiotic therapy) services not only allows improved use of hospital beds, but decreases the likelihood of patients contracting another HCAI such as norovirus or *Clostridium difficile* (*C. difficile*) infection.¹³⁴ Patients prefer to safely receive intravenous antibiotics in their own home, than to return to hospital on a sometimes daily basis. In primary care, pharmacists have also been involved in the development of delayed prescriptions where it is not clear if antibiotics are needed; 70% of patients never return for their prescription.¹³⁵ In addition, the use of minor ailment schemes whereby patients can receive symptomatic treatment for infections can decrease visits to the GP by 50% and reduce the number of prescribed antibiotics.⁷⁹

C. difficile infections are often associated with the use of antibiotics, particularly quinolones, broad spectrum penicillins and third generation cephalosporins. Pharmacists have been particularly successful in ensuring the use of these antibiotics is appropriate, thereby reducing the number of cases. In secondary care, infection control pharmacists already work across teams and networks to ensure infection management is multidisciplinary.

REDUCTION OF HOSPITAL SPREAD INFECTIONS

Clostridium difficile (*C. difficile*) is a bacterium that causes diarrhoea and more serious intestinal conditions such as colitis. *C. difficile* infections most commonly occur in people who have recently had a course of antibiotics and are in hospital. In 2009, the Scottish Government set a target to reduce *C. difficile* infections in patients aged 65 and over by 30%, by reducing 4C prescribing (i.e. the prescribing of ciprofloxacin (and other quinolones), co-amoxiclav, cephalosporins and clindamycin). In NHS Grampian, printed guidelines, posters, reminders on payslips and root cause analysis of new *C. difficile* cases were used to implement change, with lead roles in this for antibiotic pharmacists and clinical pharmacists. As a result, 4C antibiotics, as a percentage of all prescribed oral antibiotics, dropped from approximately 40% to 15% and new *C. difficile* cases from 40 to 5 per month.

CHALLENGES

45. *Ensure that currently available antibiotics are used appropriately, and encourage the understanding of good hygienic practices*
46. *Maintain the maximum effectiveness of currently available antimicrobials through antimicrobial stewardship*

3.4.3.3 Drug Misuse

PHARMACY SERVICES

The role of pharmacists in supporting drug misusers is another example where pharmacists play an important role in the protection of specific patient groups. Community pharmacists support people who misuse drugs by supplying alternatives under supervision. Community pharmacists currently make a significant contribution to the care of people with substance misuse problems through dispensing and supervising consumption of substitute opioids (e.g. methadone), and by providing needle exchange schemes to prevent the spread of blood-borne viruses.¹³⁹⁻¹⁴¹ These services are evidence based and needle exchange in particular is believed to have contributed to limiting the spread of HIV.¹⁴²

EVIDENCE SUPPORTING PHARMACY INVOLVEMENT

Pharmacy practice in the field of drug misuse research has been particularly strong, with initiatives studied to consider the effect of interventions such as training pharmacists in motivational interviewing. These demonstrated increased treatment retention and better treatment satisfaction.¹⁴³ There has been considerable research to measure the pharmacist's attitude to providing services to drug misusers and their level of involvement. This has identified that pharmacists have become more involved in dispensing for drug dependence and, to a lesser extent, needle exchange, and correspondingly more positive over time towards providing these services.¹⁴⁴ This research has demonstrated that pharmacy as a profession has been willing to manage this challenging patient group when other generalists such as general practitioners have reduced their involvement.¹⁴⁵ In addition, early qualitative research with drug misusers identified problems of stigmatisation associated with being a drug misuser. This informed both practical changes, e.g. in the development of educational materials for pharmacists, and structural changes such as the development of private areas within pharmacies. The problems of stigmatisation of drug misusers have only recently been acknowledged. Practice research continues to develop in this area with pharmacists having a role in the distribution of naloxone to prevent drug-related deaths and other initiatives to reduce drug-related harm.

CHALLENGE

47. *Build on the available evidence base to further elucidate the role of pharmacy in supporting drug misusers*

3.4.3.4 Immunisation

Historically, immunisation services have been provided by the nursing and medical professions. Increasingly, however, there is evidence that pharmacists can play an important role in disease prevention by advocating and administering immunisations.

Immunisation services initially started in the United States where pharmacists were given authority to administer vaccines under individual state laws and regulations. Pharmacists are now authorised to administer influenza vaccine in all 50 states of the United States.¹⁴⁶

PHARMACY IMMUNISATION SERVICES IN THE UK

In the UK, immunisation services from pharmacies are less well developed, but are growing rapidly. An early pilot of an influenza immunisation service was set up in Aberdeen in 2002.¹⁴⁷ Seasonal influenza immunisation is now provided in a variety of NHS settings. Several Primary Care Trusts in England and Health Boards in Scotland and Wales have now also developed local services for delivery of influenza immunisation services to those patients in one of the at risk groups or occupational health groups.

Community pharmacies are ideally situated to contribute to NHS vaccination programmes by targeting at risk individuals, for example, those identified when they present a prescription for dispensing. They have the potential to increase access and capacity to deliver on new and existing NHS immunisation campaigns in order to increase uptake rates and meet immunisation targets.

The Isle of Wight Primary Care Trust commissioned a patient evaluation of their community pharmacy influenza immunisation service, inviting feedback from over 2,000 patients regarding their experience.¹⁴⁸ The evaluation found that about 10% of the total of the patients vaccinated through all immunisation services were vaccinated by community pharmacists; over 90% of patients rated the service as excellent, and 98% would use this community pharmacy service again.

Service commissioners are also starting to examine other areas where community pharmacy can support Public Health campaigns such as pneumococcal, hepatitis B and human papilloma virus (HPV) immunisation. In Grampian, following a needs assessment, a pilot travel immunisation service was set up in 2007 in two community pharmacies.^{149,150} Following a positive evaluation the service continues to be provided. Non-NHS vaccination services

are also now widely available from community pharmacies in the UK, both from large multiple pharmacy chains and independent and small chain pharmacies.

CHALLENGES

48. *Further integrate pharmacy immunisation services into the NHS*
49. *Expand the pharmacy vaccination services to include patients in the 'at risk' categories who prefer this venue*

3.4.3.5 Surveillance of Disease and Medicines

ADVERSE DRUG EVENTS

Developments in medicines have undoubtedly improved the quality and span of life, reduced the necessity for surgery and maximised community-based care. Medication errors or adverse drug events, however, account for a substantial proportion of all health service adverse events. While one study found that adverse events associated with medicines use accounted for 6% of unscheduled hospital admissions,¹¹ research published in 2010 provided information specifically about adverse drug reactions. It was found that between 1999 and 2008 there were 557,978 adverse drug reaction (ADR)-associated hospital admissions in England, representing about 0.9% of total hospital admissions, with the annual number of ADRs increasing from 42,453 in 1999 to 75,076 in 2008.¹⁵¹ Prescribing errors accounted for a substantial proportion of all events and often caused the most significant health problems. The study results confirm that the safe use of medicines is an important aspect of public health.

SUPPORTING SAFER PRESCRIBING

Pharmacists in community and hospital pharmacy have long played an important role in preventing prescribing errors reaching the patient by contacting the prescriber to confirm their intentions, and ensuring the safe and accurate delivery of medicines to patients. In hospital pharmacy, pharmacists with clinical commitments play a particularly important role in supporting all doctors but especially junior doctors in their prescribing. Pharmacist interventions can be very effective at reducing prescribing errors. One study showed that clinical pharmacists detected errors in the medication records of a third of hospitalised patients, and by intervening prevented the errors reaching the patients.¹⁵²

Changes in the skill mix of the pharmacy dispensing team, and the increased use of automation in the supply of medicines have the potential to further improve patient safety by freeing up the pharmacist's time to concentrate on their clinical roles.

REPORTING ADVERSE DRUG REACTIONS – PROMOTING THE YELLOW CARD SCHEME

The Medicines and Healthcare products Regulatory Agency's (MHRA's) Yellow Card Scheme (YCS) enables the reporting and identification of suspected medication-related adverse reactions, of both prescribed and OTC medicines, which may be rare but potentially serious. It is widely recognised, however, that only about 15%

of all eligible ADRs are reported under the scheme. An increased culture of reporting adverse events by pharmacists would enhance the scheme. Pharmacists are also key to raising patient awareness of the YCS, encouraging them to use the recently introduced patient reporting option and supporting them to make reports.¹⁵³ Opportunities for complementary approaches to identifying new signals of adverse events, such as those offered by data linkage at a national level, need to be explored.¹⁵⁴

CHALLENGE

50. *Find new complementary ways to facilitate earlier identification of adverse events*

3.4.4 DISEASE SCREENING

EARLY IDENTIFICATION OF DISEASE

It is well established that earlier diagnosis of major diseases such as type 2 diabetes and cancer would significantly contribute to improved patient outcomes. Although many pharmacies offer services to identify patients with, for example, hypertension or diabetes, these services tend to use opportunistic testing rather than contributing to formal screening programmes. An array of robust and quick immunological analytical tests are now available that allow drugs and hormones to be detected and measured in blood and urine. These point-of-care tests are used in community pharmacy to measure, for example, insulin, cholesterol and pregnancy hormones to detect diabetes, cardiovascular risk and pregnancy.

In Scotland, Keep Well,¹⁵⁵ a national health check programme that focuses on screening for cardiovascular disease and its associated risk factors, has been introduced. It targets those in the 15% most deprived communities and in some Health Boards, community pharmacy is an equal provider with other services such as general practice. There are opportunities to develop similar services, utilising the scientific and clinical knowledge of the community pharmacist and the accessibility that the community pharmacy provides to target other diseases. Similar models of public health are being championed and evaluated across England, such as the Healthy Living Pharmacies,¹⁵⁶ alongside established public health roles in Wales.

IDENTIFYING CANCER SYMPTOMS

It is widely accepted that the early symptoms of many diseases are managed by self-treating with medicines purchased from a community pharmacy. Some diseases, however, remain largely asymptomatic until an advanced stage. Even in such instances, however, community pharmacists can play an important role in increasing patient awareness of disease and reducing delays in patient treatment. In a joint initiative organised by the Royal Pharmaceutical Society and the Roy Castle Lung Cancer Foundation in 2011, pharmacists identified and subsequently referred to general practitioners (GPs) patients whom they thought had symptoms suggestive of possible lung cancer. A similar initiative targeting bowel cancer was conducted in 2012. Further research that links pharmacy interventions to patient outcomes, however, is required, such as how many of the patients referred to GPs actually attended the GP and how many of those were diagnosed with cancer.

CHALLENGES

51. *Increase pharmacy's evidence-based contribution to earlier diagnosis of chronic disease and greater involvement in patient screening*
52. *Contribute to the evidence base evaluating the relative risks and benefits of screening for diseases*

3.5 Global Health

WORLD HEALTH ORGANIZATION (WHO) MILLENNIUM GOALS

Whilst there are health inequalities within the UK and in the developed world, the disparities globally with the developing worlds are even greater and the resources available to address these inequalities are often inadequate. In 2000, the WHO published eight Millennium Development Goals with the aim of trying to achieve them by 2015 when new goals will be set.

The eight goals, which all influence health and are interdependent, are: to eradicate extreme poverty and hunger; to achieve universal primary education; to promote gender equality and empower women; to reduce child mortality; to improve maternal health; to combat HIV/AIDS, malaria and other diseases; to ensure environmental sustainability; and to develop a global partnership for development.

3.5.1 ACCESS TO MEDICINES

Pharmacy, at a global level, is in a position to contribute to the WHO Millennium Goals through improving access to quality assured medicines and provision of pharmaceutical care. There are, however, many barriers which must be overcome. In some countries, low availability of medicines in the public sector often forces patients to purchase medicines at prices substantially higher than international reference prices. Furthermore, the pharmacist's professional activities are often compromised and undermined by the distribution of counterfeit medicines (see also 3.5.3 Managing the Health Consequences of Globalisation), the sale of ineffective remedies often related to beliefs in traditional medicine, a lack of information about medicines, a failure of countries to enforce regulations, and corruption at institutional and individual levels.

Professional pharmaceutical infrastructures must be established in all countries to improve affordable access to effective treatments for people in the developing world, and international networks must be used to share examples of good pharmaceutical care. If successfully implemented, this would contribute to the goal of equitable, quality assured distribution of medicines

and better informed local populations, thereby reducing disease and securing better population health. Furthermore, the responsible re-use of medicines presents opportunities to improve global access to medicines and improve health as well as reducing the environmental and financial costs associated with destroying medicines.

Recently, there has been a call to promote transparency and ethical practice, to introduce terms of reference and conflict of interest policies, to intensify efforts to monitor medicines prices and availability, and to improve procurement and equitable financing. In response to some of these challenges, a Health Impact Fund (HIF) has been proposed¹⁵⁷ to incentivise the research and development of new pharmaceutical products that make substantial reductions in the global burden of disease.

CHALLENGES

53. *Provide equitable access to medicines and pharmacy services to all patients globally*
54. *Minimise the barriers to the responsible global re-use of medicines*

3.5.2 REDUCING THE PERVALENCE AND SPREAD OF DISEASE IN THE DEVELOPING WORLD

Across the developing world, pharmacy infrastructure and the recognition of the pharmacy profession are highly variable, resulting in the pharmacist's knowledge and expertise frequently being underutilised.

The lack of national professional associations in many countries, as well as a lack of strategies for pharmacy and health, exacerbates medication-related problems in these countries.

MANAGING COMMUNICABLE DISEASES

Public health priorities for the pharmacy profession in the developing world will inevitably vary according to local need. One of the major global public health challenges today is the management of communicable diseases such as malaria, tuberculosis and HIV-related illness, which together account for about 56% of all global deaths due to infectious and parasitic diseases. Each year, malaria accounts for approximately a million deaths, mostly in sub-Saharan Africa, and it is estimated that 80% of malaria deaths occur in just 14 African countries.¹⁵⁸ Tuberculosis causes 1.7 million deaths each year and is especially prevalent in South East Asia and sub-Saharan Africa with these areas accounting for over 95% of deaths in developing countries.¹⁵⁹ Of those living with HIV worldwide, 67% are in Sub-Saharan Africa,¹⁶⁰ which is where 70% of the total number of deaths due to HIV-related illness occurs.¹⁶¹

THE LIVEWELL INITIATIVE, NIGERIA

AIDS can be prevented by better education and removal of its associated social stigma. In Nigerian society, as indeed in the rest of Africa, Health literacy is very low. The LiveWell Initiative in Nigeria is a pharmacy-led educational project that aims to halve health-illiteracy in Nigeria by the year 2030, and thereby increase the life expectancy of Nigerians to 70 by the year 2030. Specifically the initiative aims to improve the health status of the Nigerian people through wellness promotion, health-empowerment and positive encouragement of health-seeking behavior. The initiative aims to change the pleasure-seeking behaviour of youths and vulnerable adults by developing personal empowerment. The HIV/AIDS enlightenment programme to improve sexual health amongst the poor and vulnerable groups is just one of several initiatives which includes drug use and abuse, malaria eradication and illness poverty alleviation.

These diseases cause significant social and economic burden in the affected areas. Although these diseases are best managed by preventative measures, including lifestyle, education and immunisation programmes, medicines continue to play a key role in their treatment. For malaria, however, increasing resistance to all current drug treatments is a major problem, especially as no new drugs are known to be in development.

In contrast, the main treatment for tuberculosis involves complex regimens where pharmacists can play a key role in supporting adherence to therapy over the six month treatment course. For those infected with HIV, antiretroviral treatments given soon after infection can control the disease, but these medicines are expensive and less available to those in developing countries compared with developed countries.

IMPACT OF ZOOSES

Zoonoses are diseases that can be transmitted from animals to humans and include bacteria (*Salmonella*, *Escherichia coli*), viruses (ebola, rabies), fungi (ringworm) and parasites (toxoplasmosis). Zoonoses and diseases that have recently emerged from animals (swine flu, bird flu, coronaviruses (severe acute respiratory syndrome (SARS))) are a health problem that particularly affects those in developing countries, making up 26% of the infectious diseases burden in low income countries compared to just 0.7% in high income countries.¹⁶² The drivers for the emergence of zoonoses include climate change, increased international travel of humans and live animals, cheap food as a result of intensive agriculture and increased global trade, and the globalisation of people and markets. International surveillance and collaboration at national, European and global level are essential if the spread of zoonoses is to be minimised.

The majority of zoonoses cannot be treated in a community pharmacy setting. However, patients presenting to a community pharmacist with symptoms or a history that suggest zoonotic disease can be referred to medical practitioners. In addition, through knowledge of the patient and their domestic situation, community pharmacists can identify where chronic or acute exacerbations of conditions may be associated with zoonotic disease from a companion or other animal.

CHALLENGE

55. *Reduce the development and spread of disease in the developing world*

3.5.3 MANAGING THE HEALTH CONSEQUENCES OF GLOBALISATION

FACTORS INFLUENCING GLOBAL SPREAD OF DISEASE

Increasing globalisation impacts on many aspects of social and economic life, including health and its management. Speed of travel, increasing urbanisation and population density all facilitate the rapid spread of new diseases, as was evidenced recently by the spread of severe acute respiratory syndrome (SARS). Local outbreaks can quickly become epidemics and pandemics, e.g. influenza. Earlier recognition and identification of new diseases would reduce delays in management, either implementing preventative measures or defining suitable treatment. Better global management of pandemics would enable earlier recognition of the nature and level of threat posed by the disease, as well as allowing management strategies that are proportionate to the risk.

COUNTERFEIT MEDICINES

While the global supply chain has the potential to increase access to affordable medicines through the use of cheaper labour markets for procurement and manufacturing, this approach is not without problems. About 10% of the global supply chain is estimated to include counterfeit medicines, ranging from about 1% of medicines distributed in the developed world, about one third of those sold in developing countries to over 50% of those purchased via the internet.¹⁶³ While the parallel importing of medicines from other European countries into the UK may provide less expensive medicines and reduce short-term medicines supply problems, their use has been associated with counterfeit medicines entering the UK pharmacy wholesale network. Pharmacy

organisations, working with Government at national, European and global level, and with the support of the pharmaceutical industry, must work to introduce measures that minimise the risk of counterfeit medicines entering the medicines supply chain. Within Europe, the 'Falsified Medicines Directive' (European Directive 2001/62/EU) introduces measures to prevent the entry of falsified medicines into the legal supply chain through a range of measures, including strengthening controls and check on medicines as they move through the legitimate supply chain, on starting materials sourced from non-European Union countries and on excipients.

Pharmacy must develop a policy for international pharmaceutical public health and work within international infrastructures to improve access to safe medicines, improve population health and reduce medicines wastage. Pharmacists must be vigilant and alert to the possibility of counterfeit or falsified medicines entering the legitimate supply chain and raise any concerns with their national medicines regulatory agency. Visual or physical changes to the medicine or its packaging may be suggestive of a counterfeit or falsified medicine and care should be taken when obtaining medicines from new or alternative sources. As counterfeit medicines around the world are often detected first by patients, pharmacists should pay particular attention to any feedback from patients regarding their medicines.

CHALLENGE

56. Improve access to quality assured medicines in the developing world, including reducing counterfeiting

3.5.4 EFFECTS OF CLIMATE CHANGE ON HEALTH

IMPACT OF TEMPERATURE AND EXTREME WEATHER EVENTS

Climate change is described as the biggest global health threat of the 21st century with global warming predicted to result in a range of effects, including heatwaves, water and food shortages, and the spread of infectious diseases. Heatwaves are known to result in healthy people developing a range of symptoms from dehydration and heatstroke through to life-threatening effects on the

cardio respiratory system. A heatwave in 2003 is estimated to have resulted in the death of 70,000 Europeans. While heat-related deaths do occur in the UK, the low temperatures encountered during the winter months present a greater health burden. Globally, extreme weather events, e.g. storms and hurricanes, are expected to become more common, leading directly to increased mortality and morbidity but also flooding and associated vector- and water-borne diseases.¹⁶⁴

With small increases in global temperature it may become more difficult to control existing diseases. There is the risk that tropical diseases will spread to new areas. For example, the range of malarial mosquitoes will extend northwards into areas not normally affected by mosquito-borne infections, such as malaria and Dengue fever. In addition, conditions currently described as rare diseases that are treated by orphan drugs may become more prevalent.

In the event of a natural disaster, the International Pharmaceutical Federation (FIP) works to ensure the necessary medicines are available to the areas of need. Following Typhoon Haiyan in the Philippines in 2013, FIP co-ordinated donations from individuals and FIP member organisations, which were used to support the efforts of the Philippine Pharmacists Association in ensuring the continuous supply of essential medicines for victims of the typhoon.

FOOD AND WATER SHORTAGES

Food and water shortages predicted to occur due to climate change are expected to increase diarrhoeal disease and malnutrition. Diarrhoeal diseases kill more children than AIDS, malaria and measles combined, with about 88% of deaths due to diarrhoeal illness worldwide attributed to unsafe water, inadequate sanitation and poor hygiene.¹⁶⁵ As a consequence, access to clean water and adequate sanitation is crucial if outbreaks of water-borne disease are to be avoided.

AIR POLLUTANTS AND ULTRAVIOLET LIGHT

Levels of the respiratory irritant, ozone, known to be associated with exacerbations of asthma and chronic obstructive pulmonary disease are increasing in Europe. The burning of fossil fuels results in the air pollutants nitric oxide and sulphur dioxide, known to cause deterioration in cardiac conditions. Although higher levels of ultraviolet light may increase the risk of some skin cancers, they may also have positive health benefits in improving an individual's production of vitamin D.

MINIMISING THE CONSEQUENCES OF CLIMATE CHANGE

Pharmacy can contribute to addressing the consequences of climate change in a number of ways.¹⁶⁶ The production and distribution of pharmaceutical products are associated with a carbon footprint; the pharmaceutical industry is involved in initiatives to minimise this through the use of low carbon and renewable energy sources. As a result of environmental pressures, the use of chlorofluorocarbons in aerosols for inhalation has been phased out and alternative propellants used. These formulation changes have resulted in modifications to the dose of some inhaled medication required by patients and pharmacists have supported patients to ensure the proper use of the reformulated aerosol products following their introduction.

Pharmacists, through their daily contact with patients and the public, can provide advice on how to minimise the effects of heat through avoiding dehydration and heatstroke, and also to recognise more serious symptoms associated with excessive exposure to heat. Pharmacists also disseminate information on the effects of excessive exposure to ultraviolet radiation and how to minimise this to reduce the risk of skin cancer. Finally, to reduce further the impact of pharmaceutical products on climate change, it is essential that medicines waste is kept to a minimum.

4. DEVELOPING THE UK AS A WORLD CENTRE FOR PHARMACEUTICAL SCIENCE

4.1 Introduction

In the latter half of the 20th century the UK developed as a centre of expertise in pharmaceutical science and, in particular, in the discovery of drugs and the development and production of medicines. This activity has resulted in huge improvements to the health of the UK population through the prevention and cure of disease, and has led to improved productivity of the nation's workforce. Furthermore, the pharmaceutical industry has made an enormous contribution to the UK economy both at national and international levels.

To ensure the continuance of these economic, societal and scientific benefits, the UK must continue to be one of the world leaders in medicines research and development, and policies that promote the development of the UK as a centre for the pharmaceutical sciences must be implemented. There is also a requirement for greater education of the public around clinical trials, to encourage their wider participation in industrial, academic and public sector clinical research.

4.1.1 UK AS THE PREFERRED LOCATION FOR PHARMACEUTICAL RESEARCH, DEVELOPMENT AND MANUFACTURE

CHANGING LANDSCAPE

The pharmaceutical industry is currently dealing with an unprecedented period of patent expiration and Government cost containment, and has recently undergone a period of major mergers and acquisitions, resulting in job losses and the closure, or scaling down, of activities at UK sites. Furthermore, the environment in which pharmaceutical companies operate is complicated as they struggle with low growth in developed economies and 'super-growth' in the emerging markets.

The pharmaceutical industry is attempting to adapt to the changing landscape by seeking to encourage flexibility in all its activities and to increase and enhance diversity in its product pipelines. These developments have encouraged the adoption of new models for future innovation, such as open collaboration and increased partnership involving other pharmaceutical companies, academia and the public and private sectors.

Increasingly, larger pharmaceutical companies are acquiring new and innovative drugs and technologies from other companies, particular SMEs, or are working in partnership with smaller companies and universities to maximise the number of research and development (R&D) projects that they can advance. Universities concentrate on research around drug discovery and innovation, which larger pharmaceutical companies then use to develop more creative and innovative products. Both sides can benefit from these partnerships – small companies and universities from having their innovations marketed, while the larger pharmaceutical companies have research performed more efficiently. It is, however, essential that the larger pharmaceutical companies retain the involvement of pharmaceutical scientists with expertise in the early stages of discovery and development in order to accurately gauge the positive and negative aspects of new drugs and drug technologies being developed by smaller companies and the risks involved therein.

CONTRACT RESEARCH

The use of a contract research company to outsource a piece of development work is now commonplace within the pharmaceutical industry. 30 years ago, however, the concept was virtually unheard of when pharmacist Sir Roger Jones spotted an opportunity to set up a company to undertake contract development for the pharmaceutical industry. As a result, he formed Penn Pharmaceuticals in 1979 in the village of Penn, Buckinghamshire. The company now operates from South Wales. In addition to being one of the longest established contract companies in the world, Penn Pharmaceuticals has grown into one of the leading international contract research companies. Sir Roger has, more recently,

set up a variety of successful life science companies including Agroceutical Products Ltd (daffodil alkaloids), Bioextraction Wales Ltd (continuous countercurrent chromatography), Biofuels Wales Ltd (delignification), BioMonde Ltd, formerly ZooBiotic Ltd (maggot therapy) and Phytovation Ltd (natural products). Also realising the importance of staff training at the leading edge of technology, Sir Roger has been active in the Training and Enterprise Councils, and was Chairman of Gwent Training and Enterprise Council. In recognition of his services to the pharmaceutical industry he received an OBE in 1996 and was knighted in 2005. He was made a Fellow of the Royal Pharmaceutical Society in 2009.

Despite these constraints, and the increasing competition from other global markets, the UK is well placed to compete. It retains its pre-eminent position with regard to pharmaceutical sciences, particularly if measures are put into place to encourage pharmaceutical companies to base themselves in the UK, as well as supporting innovation and development in new medicines. These would include new models for payment once a medicine is licensed.

CHALLENGES

57. *Ensure the UK remains an attractive location for the pharmaceutical industry to undertake medicines research and development*
58. *Encourage greater collaboration amongst large pharmaceutical companies, SMEs and universities to support drug discovery and medicines innovation*

NEW AND INNOVATIVE MEDICINES

The pharmaceutical industry invests more in R&D than any other industrial sector, with the Association of the British Pharmaceutical Industry (ABPI) reporting that this amounted to 28% of all commercial research and development carried out in the UK in 2011,²⁰ equating to a spend of £4.85 billion on industrial pharmaceutical research and development in 2011. This inward

investment not only provides employment opportunities for UK graduates, including pharmacists and pharmaceutical scientists, but also feeds through to the funding of teaching and research in the higher education sector.

Research and innovation occur not only in pharmaceutical companies whose major focus is the development of new drugs as medicines but also in pharmaceutical companies whose primary focus may be, for example, generic medicines, line extensions, topical products or biosimilars, where developments need to be underpinned by a significant science-based input.

There are, however, currently a number of serious threats to the maintenance of a strong pharmaceutical R&D base in the UK. In order to ensure that it remains competitive, there must be stronger support from the UK Government, regulatory agencies, NICE, SMC and AWMSG for policies that encourage innovation and the timely development of new, cost-effective and clinically effective medicines.

In this context, the MHRA has introduced many initiatives aimed at improving timings, reducing delays, removing bottlenecks and minimising unnecessary and inconsistent checks at a national and European level. These include the revision and simplification of the European Union Clinical

Trials Directive. Furthermore, the MHRA has recently established an Innovation Office to facilitate discussion between industries, academia and regulators on new and innovative medicines, medical devices and medical technologies. The Innovation Office builds on the well-established national and European systems for provision of scientific advice to companies. Indeed, the UK is one of the leading proponents of scientific advice in the EU, making a major contribution to the development programmes, and is able to influence the decision-making processes that take place in industry. The UK's MHRA has been able to establish this prominent position through the pharmaceutical science base that is inherent in its scientific staff.

CHALLENGE

59. Support the UK pharmaceutical industry to remain a major and competitive player in global research and development

DEVELOPING NEW QUALITY PROCESSES

Quality by Design (QbD), Process Analysis Technology (PAT) and design space are examples of initiatives that enable pharmaceutical companies to better understand their product and the process by which it is made, as well as the impact of critical material attributes and process parameters on safety and efficacy. As a consequence of this better understanding, it should be possible for pharmaceutical companies to reduce waste (e.g. the number of failed re-worked batches of medicines) associated with sub-optimal and/or poorly understood/poorly controlled manufacturing processes and may ultimately result in reducing end product testing. Such initiatives also have the potential to remove the requirement to file for product variations.

The concept of QbD is not new and its development has, in part, been driven by the FDA and US industry. It has been practised for many years through the design of experiments in a number of aspects of the medicines development process, e.g. process definition, formula selection and optimisation, and process validation. The widespread adoption of QbD working practices should increase efficiency and reduce waste in the pharmaceutical industry, producing medicines of a higher quality, and assure a consistency of supply, leading to fewer recalls and shortages.

QbD is, however, expensive to implement and requires highly skilled personnel, and to date the inclusion of QbD in regulatory submissions has been limited. Thus far, the

regulatory agencies have only issued guidance on QbD, so conformance with the requirements is not mandated, although it is embraced within the International Conference on Harmonisation Tripartite Guideline on Pharmaceutical Development (ICHQ8).

CHALLENGES

- 60. Encourage medicines regulators in the UK and EU to promote Quality by Design (QbD)-enabled development programmes and filings*
- 61. Develop medicines licensing processes that enable timely changes to materials, manufacturing processes and analytical test methods arising from continuous improvement initiatives*

EMERGING MARKETS

At the most applied end of the pharmaceutical sciences spectrum, there is a need to improve manufacturing efficiency if the UK pharmaceutical industry is to remain competitive with the rapidly expanding markets such as the BRIC (Brazil, Russia, India, China) economies. Indeed, the majority of drugs or active pharmaceutical ingredients (APIs) and medicines on the European market are now manufactured in Asia with India and China being major exporters to the EU. Low employment and capital costs are driving pharmaceutical development activities to these emerging markets, in particular the generic market in India and the manufacture of active pharmaceutical ingredients in China. This competition from science bases in Asia and the comparatively cheap labour are current realities and future threats to the UK industry and to the provision of healthcare products to UK patients.

As a consequence of importing APIs and medicines, there are a number of serious threats to maintenance of the supply chain. These threats include: quality issues of drugs and medicines, changes to the importation of APIs from countries outside of the EU, 'skimming' operations where medicines are exported rather than made available to UK patients, and falsified or counterfeit medicines. Concerns about quality issues are now being addressed by expanded approval API certifications and good distribution practice guidelines, while the Falsified European Medicines Directive will introduce a number of measures that aim to address some of these shortfalls.

CHALLENGE

- 62. Maintain the integrity of the medicines supply chain in the UK through joint working of all stakeholders.*

OPPORTUNITIES IN EMERGING MARKETS

While there are opportunities for the UK pharmaceutical industry in the BRIC economies, different healthcare models for marketing authorisations, pricing, reimbursement and distribution exist in these countries. Thus, a different value proposition has to be provided in that the industry must supply affordable medicines, as patients in these economies cannot afford expensive medicines such as monoclonal antibodies.

MEDICINES REGULATION

From a regulatory standpoint, the pharmaceutical sciences must proactively inform organisations like the FDA, European Medicines Agency (EMA) and MHRA of scientific advances that impact directly on the medicine approval process. The pharmaceutical industry and academia have a role to play in developing and validating approaches by which the regulatory burden on the development of medicines can be alleviated and the time from discovery to marketing reduced. This point is especially pertinent for the new 'biologics', which are being increasingly submitted to the regulatory agencies. The risk-based approaches for inspection and assessment operated by the MHRA and other regulators must be proportionate but must not stifle future innovation and developments.

The revision and clarification of the regulatory systems by the UK and the rest of Europe regarding the requirements and conditions for post approval changes, as well as the 'do-and-tell' and 'tell-and-do' notifications, have removed some of the need for formal approval of changes. Many of these changes are administrative processes rather than requiring prior scientific evaluation before implementation. The MHRA is also committed to make urgent changes under the Batch Specific Variation scheme to help maintain the supply chain.

In summary, regulations which govern clinical trials, patent protection and marketing authorisations for medicines not only have a bearing on the pace of medicines innovation, they also play a critical role in the attractiveness of locations for the pharmaceutical industry. Medicines regulation in the UK must be proportionate and not act as a disincentive to any pharmaceutical company wishing to operate in the UK, whilst maintaining patient safety.

CHALLENGE

63. Develop novel regulatory systems that expedite the marketing authorisation process for innovative therapies

MEDICINES COSTS

If patients are to continue to receive new and innovative medicines, the NHS and the pharmaceutical industry will need to develop a new relationship based on partnership and not just on transactions. The pharmaceutical industry must understand the impact that any NHS restructuring has on commercial models and evolve accordingly. The increased use of risk sharing (patient access) schemes will require a better understanding of the intrinsic value of new medicines coming onto the market. Furthermore, as product value will have to be demonstrated, both clinical and economic evidence will have to be made available. A model being considered (although not yet introduced) by the UK Government, and supported by NICE, is value-based pricing⁶⁷ which aims to strike a balance between delivering reasonable prices for the NHS and ensuring that the pharmaceutical industry is incentivised to undertake research to develop and market new and improved medicines. Under this scheme, the price the NHS pays for a new medicine will be based on the benefit it brings to patients when measured against other available treatments. The scheme, however, is not just about new and innovative medicines – it also involves aspects of the economics of healthcare provision and funding impact as well as generic prescribing and NHS contracts.

CHALLENGE

64. Develop new NHS models of medicines reimbursement that give patients timely access to new medicines, while enabling the pharmaceutical industry to invest in future medicines innovation

An understanding of the current serious position the UK-based pharmaceutical industry faces from global competition is needed to ensure the UK remains the preferred location for the pharmaceutical industry. There are increasing examples of harmonisation practices and work-sharing across Europe which seek to reduce duplication of effort, increase efficiency and achieve ultimate consistency of decisions. The Government must create a competitive business environment in terms of making the UK more financially attractive to companies, reducing any unnecessary regulatory burden and investing in scientific education and skills.

4.1.2 UK AS THE PREFERRED LOCATION FOR CLINICAL RESEARCH

The pharmaceutical industry provides pharmaceutical scientists with the opportunity to participate in the design and implementation of clinical studies, ensuring that these professionals remain at the cutting edge of clinical research and pharmaceutical science to the benefit of patients.

REDUCED PARTICIPATION IN CLINICAL TRIALS

In 2011, the Academy of Medical Sciences reported¹⁶⁸ that in 2002, 46% of EU products in clinical trials were being developed in the UK. By 2007, however, this had fallen to 24%. MHRA data indicated that the number of trials approved between 2004 and 2008 was unchanged but the UK global market share of patients participating in trials dwindled from 6% to less than 3%. Furthermore, half of the representatives of major pharmaceutical industries surveyed in 2008 expected to reduce the number of clinical trials in the UK. Commercial and non-commercial researchers alike indicated that the complexity of the regulation and governance pathways limited their research.

INITIATIVES TO INCREASE PARTICIPATION IN CLINICAL TRIALS

A number of initiatives aim to reverse this trend. The Health Research Authority (HRA) was established in December 2011 as an NHS Special Health Authority. In addition to protecting and promoting the interests of patients and the public in health research, the HRA works with the Medicines and Healthcare Regulatory Agency (MHRA) and the National Institute of Health Research (NIHR) to create a streamlined consistent national system of research governance for clinical trial approval, compliance and inspection.

The NIHR has created a unified health research system within the NHS by coordinating and funding research in England. Through Clinical Research Networks, improvements have been made to the initiation, conduct and delivery of research together with significant improvements in participant recruitment levels. Parallel efforts exist in Scotland and Wales together with cross-border collaboration to facilitate UK-wide studies.

Community pharmacists can advise on the practical aspects of delivering trials from community pharmacies at the study design stage. In addition, they can identify

suitable study participants, obtain patient consent and store and deliver clinical trial medication. GlaxoSmithKline has recently involved community pharmacies in the Salford area of Greater Manchester in a phase 3 clinical trial to assess the clinical effectiveness of a new combination therapy and inhalation device for the treatment of asthma and chronic obstructive pulmonary disease.

CHALLENGE

65. Increase the number of patients participating in clinical trials in the UK

IMPACT OF THE EU CLINICAL TRIALS DIRECTIVE

The conduct of clinical trials for investigational medicinal products is regulated by rules set out in the European Union 'Clinical Trials Directive' (2001/20/EC). This well-intentioned legislation is, however, considered to have regulatory requirements that are disproportionate to risks, high costs and a lack of harmonisation of applicable rules for the conduct of multinational clinical trials. The bureaucratic hurdles created by the EU Clinical Trials Directive, not least in the requirement to apply Good Pharmaceutical Manufacturing Practice to the manufacture of clinical trial supplies, has contributed to a 25% decline of clinical trials in the EU between 2007 and 2011. As a consequence, many commercial Phase I clinical trial centres and their supporting pharmaceutical manufacturing units have closed.

The European Commission has now proposed a regulation to replace the existing EU Clinical Trials Directive, which should have the effect of streamlining and harmonising the approvals and reporting procedures, improving transparency and developing a regulatory framework proportionate to risk. This is critical to strengthen Europe's competitive position as a global player for translational research and the clinical development of medicines.

It is essential that pharmacists and pharmaceutical scientists engage with these initiatives to streamline the regulation and governance of clinical trials. Pharmacists in the NHS are key participants in the work of NIHR Clinical Research Networks and have an essential role in helping to meet the ambitious targets for clinical trial performance. The damage done to the UK and EU

clinical trials infrastructure, due to overregulation and bureaucratic governance, will take time to repair and pharmacists and pharmaceutical scientists will have an important role in the rebuilding of confidence and competitiveness.

AVAILABILITY OF CLINICAL TRIAL DATA

Law requires transparency between the pharmaceutical industry and regulatory agencies, e.g. MHRA and EMA. Recently, two high profile cases (Roche and Tamiflu; GlaxoSmithKline and Seroxat) involving a lack of transparency alleging concealment of findings thought to be in the public interest have stimulated a public campaign called AllTrials. Its goal is to place all clinical trials data in the public domain. The AllTrials website has called for the registration of all clinical trials, whether undertaken by industry or in the public domain (such as academia) and the publication of full methods and results within a short time after their completion. The Royal Pharmaceutical Society is a signatory to the AllTrials petition which calls for patient level data (appropriately

anonymised) and clinical study reports to be posted on the EMA websites after regulatory approval.

The wider availability of patient-level data (not part of the AllTrials campaign) requires further consideration. There can be no doubt that patient confidentiality must be assured before data can be provided in a form that can be readily processed by suitably qualified statisticians. It is essential that statistical processing is conducted in a competent manner in the public interest and to reassure pharmaceutical industry sponsors that the analysis of clinical trials will be handled objectively and responsibly. It is likely that well-resourced and funded organisations like the Cochrane Collaboration are best placed to conduct an arms-length analysis on behalf of the public and the clinical community (which includes pharmacists and pharmaceutical scientists).

CHALLENGE

66. Develop processes that ensure transparency in clinical trials and that the publication of all clinical trial data is available in the public domain in a suitable format

4.1.3 UK AS THE PREFERRED LOCATION FOR PHARMACY-FOCUSED HEALTH SERVICE RESEARCH

IMPACT OF HEALTH SERVICE RESEARCH ON PHARMACY

Health service research conducted in the pharmacy setting is referred to as pharmacy practice research. It is central to inform new policy for the profession, confirm the value of existing policy, identify gaps in provision of service and sub-optimal care, and overall to demonstrate and quantify the added value pharmacists bring to patient care.

The UK hosts some of the world-leading groups of pharmacy practice researchers, who have contributed significantly to the evolving nature of pharmacy practice. For example, services now core to community pharmacy such as repeat dispensing¹⁶⁹ and smoking cessation¹³⁹ evolved from randomised control trials conceived and conducted by UK pharmacy practice researchers.

FUNDING OF HEALTH SERVICE RESEARCH

As the parent discipline of health service research continues to develop methodologically, the standards and resources required to deliver substantive and rigorous RCTs in pharmacy continually increase. Whereas previously small research awards have supported important feasibility studies, substantive funding is now required to support the development of large scale intervention studies which have become the gold standard for evidence-based decision making.

Research Councils and other major funding bodies should be alerted to the increasingly central role pharmacy plays in healthcare delivery and include pharmacy-related areas in their lists of strategic priorities. Capacity building is also essential for maintaining the pipeline of academic and practice-based researchers, so that the UK can retain its leading role in pharmacy practice research. The newly established Pharmacy Research UK has a central role in this agenda, but it needs to link closely with universities and the new Academic Health Science Centres/Academic Health Science Networks and their equivalents in the

devolved nations to deliver this agenda. There is also a need to ensure that practice research is seen as a core activity for all community and hospital pharmacists, either through participation in large definitive studies or through small projects systematically exploring aspects of their own practice.

MULTIDISCIPLINARY WORKING

Finally, and essentially, pharmacy practice research must draw even more closely on other academic disciplines. This would include health economics to identify the best

outcomes, health psychology to ensure appropriate behavioural models are adopted to explain and predict professional and patient behaviour, sociology to explain how people and populations behave, epidemiology to make appropriate use of large datasets, and statistics to ensure results of studies are appropriately analysed and interpreted.

CHALLENGE

67. Support well-conducted pharmacy-based intervention studies conducted in line with the MRC Framework

4.1.4 FUNDING

Stakeholders with an interest in the pharmaceutical sciences, as well as the pharmaceutical and biotechnology industries, have a 'duty of care' to argue that the pharmaceutical sciences must represent a key strategic area for government and large charity funding. Indeed there may be an argument for closer collaboration between the Government, the pharmaceutical industry, funding bodies and charities regarding the future funding of the pharmaceutical sciences as outlined in the Government's Strategy for UK Life Sciences.¹⁷⁰ One example of this is the announcement in 2011 of AstraZeneca forming a partnership with the UK Medical Research Council to allow academic researchers to work on compounds discovered by AstraZeneca.

Equally, the industries underpinned by the pharmaceutical sciences must recognise that the return on investment for contributing to innovative research conducted outside their own organisations is considerable and that they have an essential role to play as co-funders with, for example, the Research Councils UK (RCUK). Other mechanisms of underwriting pharmaceutical research may also be identified, and the public-private partnership is perhaps one model that might be exploited to a greater extent than at present.

CHALLENGE

68. Strive for adequate funding to support research in all aspects of the pharmaceutical sciences

4.2 Workforce Intelligence: Planning for a High Quality Workforce

4.2.1 INTRODUCTION

Pharmacy is a unique discipline that relies on the integration of pharmaceutical science and the practice of pharmacy to optimise therapeutic outcomes for the ultimate benefit of the patient. A pharmacy education aims to produce experts in the science and use of medicines, producing health professionals who understand their role as scientifically-based clinical professionals. The science underpinning pharmacy is vast and it is imperative that pharmacy students continue to be taught the important underpinning pharmaceutical science that will allow them to work as competent professionals in their chosen field.

Most pharmacists work in the NHS within hospital pharmacy, community pharmacy or other primary care settings. Changes in NHS policy over the last decade in England, Scotland, Wales and Northern Ireland, increased patient need for medicines and consumer demand, technological developments, market and organisational changes, and government legislation have all created opportunities for such pharmacists to work differently. The recent drive for pharmacists to improve public health outcomes through enhanced pharmacy services, such as NHS health checks, sexual health services and the establishment of healthy living pharmacies (HLPs), exemplify the growing demands being placed on pharmacists to perform additional clinical roles. While the changes have mostly been welcomed, they have required enhanced skills and knowledge from individual practitioners. This has arguably resulted in the intensification of work, undermined the viability of smaller businesses and affected the way professional groups work together. These will all alter both the supply of, and need for, trained pharmacists and their employability.

Although the majority of pharmacists work in a clinical role within the NHS, a not insignificant number of pharmacists work in university departments (academia), the pharmaceutical industry, medicines regulation, and hospital manufacturing and aseptic services. Their broad understanding of medicines development and their patient awareness are invaluable. Indeed, many pharmacists working in industry, academia and in regulatory roles will have spent time during their career

in hospital and community pharmacy settings. This varied experience brings important insights into the use of medicines to their other roles. Workforce intelligence, i.e. information that supports workforce planning, is vital to make the case for increased resources, support, and training and development opportunities.

THE PHARMACY WORKFORCE

'Workforce development' in its broadest sense has been a key theme for the NHS for some time; the publication of the NHS Plan in 2000, and the pharmacy White Paper that followed, provided an impetus to professions delivering care to patients to re-focus attention on staff doing the work involved in the profession. The pharmacy profession responded in a number of ways: a research agenda around the pharmacy workforce was identified;¹⁷¹ the first census survey of the work arrangements of all registered pharmacists was commissioned;¹⁷² and a pharmacy workforce planning and policy advisory group was established, culminating in the development of an analytical pharmacy workforce model.¹⁷³ More recently, a number of independent academic research studies have advanced knowledge and understanding of the working lives of pharmacists and other members of the pharmacy team, with studies examining workforce composition and deployment patterns,¹⁷⁴ attrition,¹⁷⁵ career expectations,¹⁷⁶ job satisfaction,¹⁷⁷ international migration,¹⁷⁸ work patterns,¹⁷⁹ including locum and flexible working,¹⁸⁰ skill mix,¹⁸¹ workload,¹⁸² performance,¹⁸³ professionalism¹⁸⁴ and the use of incentives on behaviour.¹⁸⁵

FURTHER WORKFORCE RESEARCH

Despite the advances made in knowledge about pharmacists and how and where they are employed, there are still gaps in our understanding. For example, much remains to be explored with specific groups of pharmacists or some key employment topics, such as recruitment, retention, staff development and job commitment. More importantly perhaps, in a rapidly changing NHS where improving health and preventing disease within a context of declining resources will be a key challenge, the pharmacist's contribution and their effectiveness in delivering high quality healthcare will need to be more

clearly described and evaluated. A greater understanding of the difference pharmacists make to patients is required. It will be important to decide how pharmacy students and qualified pharmacists should be educated and trained to keep pace with healthcare and other pharmaceutical developments. It will also be important to understand the contribution made by pharmacists who do not have clinical roles and who work outside the NHS. Although there are too many challenges and opportunities facing the pharmacy workforce to mention, a number of issues

require more immediate attention than others because they are likely to have a huge impact on the profession's ability to deliver appropriate, timely and effective services to patients and the public. These include: workplace pressures currently being experienced by individual practitioners that may affect future workforce supply; identifying and managing demand for pharmaceutical expertise; and measuring the effectiveness of the pharmacy workforce.

4.2.2 CAUSES OF WORKPLACE PRESSURES

STRESSORS IN THE WORKPLACE

Workplace pressures are thought to be increasing. It is widely accepted that stressors at work influence employees' well-being (i.e. psychological health, physical health, job satisfaction). Well-being, in turn, can influence individual and organisational performance. Pressure associated with the expanding volume of work, for example, has been directly linked to the occurrence of dispensing errors. To prevent errors in the workplace we need to understand how and why they happen, what their impact is on patient care and on the pharmacist's well-being, and what sort of interventions can be made to alleviate pressures that lead to problematic performance.

FACTORS CONTRIBUTING TO WORKPLACE PRESSURE

Recent changes in the regulation of pharmacies, growing expectations for delivering services under the new general pharmaceutical contract, changing ownership structures, new shift patterns and the effect of long working

hours, deteriorating working conditions, staff shortages, erratic working and the long distances some pharmacists travel to work are also thought to be having an effect on performance and well-being.¹⁸⁶ In the hospital sector, workplace pressures are similarly thought to be increasing and jeopardising patient safety, with particular concerns around staffing levels, interruptions and dispensary workload.¹⁸⁷ The evidence that workplace pressures in pharmacy are significant and might be increasing requires corroboration, since most of it is anecdotal or derived from small scale exploratory studies; research into interventions which might help to alleviate those pressures, thus increasing the pharmacist's well-being and enhancing individual and organisational performance, is urgently required. Research also needs to be undertaken to determine which roles, traditionally undertaken by pharmacists, could be undertaken safely by less qualified staff, thus relieving workload pressures.

CHALLENGE

69. *Identify the causes of and solutions to workplace pressures*

4.2.3 IDENTIFYING FUTURE GLOBAL DEMAND FOR PHARMACEUTICAL SERVICES AND EXPERTISE

FUTURE SUPPLY OF PHARMACISTS

To ensure the appropriate supply of pharmacists and to meet the future and changing demands society may make of them, we need to ensure we have accurate and up-to-date intelligence about who they are, what they do currently and what they aspire to do in the future. This needs to be carefully judged against society's needs,

so that resources are appropriately allocated and channelled; in this way, demand for pharmaceutical expertise and services also needs to be identified and mapped. This should acknowledge the plurality of pharmacy expertise, extending as it does into areas of practice that fall outside the NHS.

PHARMACISTS WORKING ARRANGEMENTS

The majority of pharmacists have clinical roles within the NHS and work in community pharmacies, in hospitals or primary care organisations; a sizeable proportion work in a number of other settings, including industry and academia, and some hold down more than one post or work in more than one sector.¹⁸⁸ The growing tendency for part-time and flexible working is of particular note. The demographic characteristics of pharmacists are also altering.

Research has identified that women not only make up the majority of the current workforce, but that their representation in the profession is increasing and they have very different work patterns and career expectations compared with the diminishing number of men who qualify as pharmacists.¹⁸⁹ So, while there is an evolving infrastructure within which the profession functions, the demographic profile of the profession is also evolving. Identifying and predicting the demand for pharmaceutical expertise across all sectors and employment markets is not straightforward, but it must be a priority to ensure that it can be managed and balanced against supply. While a growing and not inconsiderable volume of research exists about pharmacists, comparable information on pharmaceutical scientists is not available.

SKILL MIX IN PHARMACY

Questions around skill mix, both vertical and horizontal, will impinge on any discussions about demand since the utilisation of technology or support staff in the pharmacy workplace for example, or role changes in other healthcare professions, will inevitably shape demand for pharmacists.¹⁹⁰ Demand for other pharmacists or pharmaceutical scientists will be measured differently and must be considered alongside demand for practitioners with clinical roles. Demand measures must also be dynamic and responsive to current and new policies. For example, the expansion over the last decade in Higher Education Institutions offering the MPharm degree programme raised demand for pharmacists with teaching qualifications.

PROPOSED CHANGES TO PHARMACY EDUCATION AND TRAINING

Similarly, the Department of Health's Modernising Pharmacy Careers (MPC) proposals for reform of pharmacist undergraduate education and pre-registration training, i.e. moving to an integrated five-year programme, may make English universities less attractive for international students, reducing student numbers further. On the other hand, plans for reform suggest that there will be an increase in the amount of work-based learning and exposure to clinical practice during the undergraduate curriculum, which may increase demand for clinical academics and greater contact with NHS and community pharmacy employers.

Traditionally, few pharmacists have been attracted to academic careers and many of those involved in teaching at an undergraduate level are not pharmacists. The review of pharmacist undergraduate education and pre-registration training recognised that a significant increase in the number of pharmacists entering academic life and pursuing academic careers would be required to deliver the MPC Board's vision for reforming pharmacist undergraduate education and pre-registration training. Major areas for workforce development include teaching, learning, assessment, curriculum design and quality assurance. This is in addition to research, to develop and oversee clinical and professional assessments and provide support and guidance to work-based assessors and tutors from within schools of pharmacy.

The review of post-registration education and training in pharmacy highlighted the lack of data on the current size of the pharmacist academic workforce and the number of pharmacists with experience of teaching in higher education that would be required to ensure that pharmacist undergraduate education and pre-registration training delivers the required outcomes.

Both reviews highlighted the importance of developing the clinical academic workforce in pharmacy and increasing research capacity, both in academia and in the wider workforce, in order to drive innovation and increase the availability of high-quality evidence to promote the adoption of best practice.

PHARMACISTS IN ACADEMIC CAREERS

The deterrents for a clinical academic career as a pharmacist are similar to those identified in other professions and include: the lack of a clear route of entry to an academic career; the lack of a transparent career structure; the lack of flexibility in the proportion of time that can be spent practising as a pharmacist while undertaking training for an academic career; and a shortage of properly structured and funded posts. In addition, there is a lack of salary-based schemes for pharmacists wishing to combine clinical and academic work or to include research as part of a broader portfolio.

Creating more opportunities for pharmacists with clinical roles to see research as a relevant and feasible part of day-to-day practice is important. Community pharmacies can be involved in supporting the delivery of research as part of their day-to-day practice. To further this agenda, Research Ready accreditation has been developed to support community pharmacy teams to understand what their responsibilities are when they get involved in research. It is a site accreditation scheme for community pharmacies that wish to quality assure their research practice. It demonstrates to colleagues in industry and academia as well as their patients and the public that their day-to-day involvement in research meets the basic requirements for participating in health research and trials in the UK (in line with Research Governance Frameworks).

PLANNING FOR THE FUTURE PHARMACY WORKFORCE

Ensuring that education and training and workforce planning support the delivery of high-quality services for patients are an important part of the role of the MPC programme overseen by the MPC programme board. This programme board sub-committee advises the Secretary of State on careers, education, and training and workforce planning for a number of health professions, including pharmacy. Under MPC a project advisory group, established to review and update an earlier pharmacy workforce model, has reported there might be a potential supply imbalance between pharmacist undergraduate numbers and pre-registration trainees posts which, unless action is taken, may result in undergraduate student numbers exceeding the number of placements available. Balancing student intake with the need for qualified pharmacists will need to be actively managed and should involve all stakeholders. So while considerable headway in planning the pharmacy workforce has already been made, it should remain a strategic objective for the Health Departments, the Royal Pharmaceutical Society, the General Pharmaceutical Council (GPhC) and other key stakeholders in pharmacy to liaise with and share intelligence with the Centre for Workforce Intelligence (CfWI), the recently established English authority on workforce planning and development, providing advice and information to the NHS and social care system. Similar agencies in Wales, Scotland and Northern Ireland should also consider workforce planning for their pharmacy workforce. Data on staffing levels, the performance, deployment, distribution, mobility and working patterns of pharmacists, and the 'softer' data on employees' motivation and attitudes towards work, should be collected on a regular basis.

CHALLENGE

70. Identify future demand for pharmaceutical services and expertise globally, including qualified persons (QPs), clinical pharmacologists, academics, locum pharmacists and pharmaceutical scientists

4.2.4 MEASUREMENT OF THE EFFECTIVENESS OF THE PHARMACY WORKFORCE

A simple definition of effectiveness is 'doing the right thing'. Being effective means producing powerful effects and involves achieving goals that support a particular vision and mission. It is not to be confused with 'efficiency', which is another term for cost-effectiveness in this context.

IMPROVING HEALTH OUTCOMES

Despite publication in 2005 of the DH vision and strategy for pharmacy 'Choosing health through pharmacy: a programme for pharmaceutical public health 2005–2015', evidence that pharmacists, their staff and the premises in which they work improve health outcomes and reduce health inequalities is still very mixed. For example, a systematic review of pharmacy-led medication for older people showed no effect on reducing mortality or hospital administration in older people.¹⁹¹ Conversely, Koshman *et al* in 2008, however, drawing on findings from a systematic review of RCTs evaluating the impact of pharmacist care activities on patients with heart failure, found that pharmacist care was associated with significant reductions in the rate of all-cause hospitalisations.¹⁹²

CHALLENGES IN DEMONSTRATING EFFECTIVENESS

Choosing an appropriate outcome, matched to the objective of the pharmacy intervention, is fundamental to study design. Holland *et al*¹⁹¹ studied the effect of a post-discharge intervention by community pharmacists delivered to patients with heart failure. It used hospital re-admission as the primary outcome against which the intervention was being judged as successful or not, with re-admission interpreted as a negative outcome. The exact causes for the re-admission were not explored, and other outcomes which might have explained the effect were not included. Two possible reasons, suggested by the authors of the study, were that either patients' better understanding of deterioration in their condition led to them seeking re-admission more quickly or that improved adherence to their medicines led to iatrogenic disease.

This study illustrates the difficulty the pharmacy profession faces when trying to establish its effectiveness. It is partly methodological, in that designing studies that sufficiently capture the relative input and contribution of pharmacists against appropriate outcomes is challenging. But it is also about being explicit about pharmacists' roles and what they are expected to achieve when performing that role. Their public health role is potentially enormous, but without defining expectations about what impact we expect pharmacists to have on patients, measuring their effectiveness in that role is impossible.

RESEARCH INTO EFFECTIVENESS

A research agenda into the impact of pharmacists on health should be articulated. A recent editorial in the *European Journal of Hospital Pharmacy* has highlighted the need to demonstrate effectiveness and value of pharmacy practice and called for closer alignment between hospital pharmacy and academia. This also needs to include assessing the pharmacist's effectiveness in other roles. Concerns that are currently raised include the effectiveness of pre-registration tutors, especially in light of the many changes taking place in MPharm curricula and changes in practice in different sectors of the profession. The effectiveness and performance of locum pharmacists is regularly questioned, and the achievements of pharmacists in specialist roles have received very little attention. To ensure pharmacists' roles are recognised and valued alongside other members of the healthcare team, their independent contributions need to be identified and their effectiveness and cost-effectiveness measured.

CHALLENGE

71. *Measure the effectiveness of the entire pharmacy workforce*

5. IMPLEMENTING NEW MEDICINES, BETTER MEDICINES, BETTER USE OF MEDICINES

5.1 Introduction

The Royal Pharmaceutical Society is fully committed to ensuring that UK pharmaceutical science remains world leading and continues to contribute to the health and wealth of the nation. **New Medicines, Better Medicines, Better Use of Medicines** presents the view of the Royal Pharmaceutical Society's Pharmaceutical Science Expert Advisory Panel on the current state of pharmaceutical science and identifies areas for development, expansion, change and innovation for the future. As with any field of science, there will be developments in pharmaceutical science that cannot be predicted at this point in time, some of which may impact on the priorities.

Pharmaceutical science is a very broad discipline and the infrastructure to support all areas of pharmaceutical science is complex; it includes a wide range of stakeholders, specifically academia, the pharmaceutical industry, Government, regulatory agencies, funding bodies, professional organisations, patients and the public. While the majority of stakeholders are UK based, the global nature of pharmaceutical science means that there are a number of European and international stakeholders.

During the preparation of the **New Medicines, Better Medicines, Better Use of Medicines** document, valuable contributions were made by many stakeholders, with several offering support for the aims of the document, assistance with its implementation and opportunities for collaborative working. Stakeholders viewed the Guide as a reference source they could use to inform and to advise, and to identify developments and areas of innovation. They also fed back that it was a resource that could be used in strategic planning and to catalyse change.

IMPLEMENTATION OF THE GUIDE

Given the wide ranging Recommendations and Challenges included in the document, it would not be possible for the Royal Pharmaceutical Society's Pharmaceutical Science Expert Advisory Panel and National Pharmacy Boards working alone to implement them. Rather the support and collaboration of stakeholders will be essential if the changes envisaged in the Recommendations and Challenges are to be successfully effected.

5.1.1 WORLD-LEADING PHARMACEUTICAL SCIENCE

To ensure that UK pharmaceutical science continues to be world leading requires the identification of gaps in the current knowledge and evidence base and a desire to undertake excellent research to address these deficiencies, as well as the creation of an environment whereby creativity and innovation are positively

encouraged and therefore prosper. In addition to the greater investment in new innovation and technologies required to achieve these goals, there is a need for greater multi/interdisciplinary working amongst stakeholders to ensure that safe, new and innovative medicines rapidly reach the patient.

5.1.2 EXCELLENT PHARMACEUTICAL SCIENTISTS

Pharmaceutical scientists require a range of skills to deal with the rapidly developing scientific and professional landscape, as well as a commitment to lifelong learning to ensure they remain at the forefront of their discipline. While academia and the workplace, which includes the pharmaceutical industry and the NHS, play major roles

in developing the pharmaceutical science workforce, the Royal Pharmaceutical Society Faculty provides pharmaceutical scientists with the opportunity to demonstrate their level of attainment and their stage of development throughout their careers.

5.1.3 IMPLEMENTATION OF THE RECOMMENDATIONS

From amongst the seven Recommendations listed at the start of the Guide, the Royal Pharmaceutical Society has identified targets that it is particularly keen to see progress and on which it will lead, working with other interested stakeholders. It will work on many of the other themes contained within the Recommendations with other stakeholders to ensure that they are developed and progressed. For some of these Recommendations it will be possible to make progress in the short term, i.e. 12 to 24 months, while others are much longer term projects and will require time scales of 5 to 10 years.

The themes on which the Royal Pharmaceutical Society will lead are listed below:

RECOMMENDATION 1 – ENSURING THE SAFE USE OF MEDICINES

- Promote further research into the causes of medication errors in patients and research into interventions to reduce those errors
- Improve patient understanding of the risks and benefits of their medication.

RECOMMENDATION 2 – IMPROVING ANTIMICROBIAL STEWARDSHIP AND STIMULATING NEW ANTIMICROBIAL DEVELOPMENT

- Educate the public and patients on the use of antimicrobials and their place in therapy

- Encourage further development of antimicrobial stewardship by healthcare professionals to maintain the effectiveness of current and any future antimicrobials.

RECOMMENDATION 3 – ADOPTING NEW TECHNOLOGIES

- Educate the public and patients about the ethical and moral issues surrounding the use of new technologies and medicines such as gene therapy, regenerative medicine, therapeutic vaccines and stratified medicine.

RECOMMENDATION 5 – INCREASING THE EVIDENCE BASE FOR PHARMACY

- Demonstrate the clinical and cost effectiveness of NHS pharmacy services by means of well-conducted, definitive trials that are appropriately funded to enhance the role of pharmacy in the treatment of patients
- Increase the health services research expertise within the profession.

5.2 Proposed Implementation Plan

Given the broad nature of the pharmaceutical sciences, it is inevitable that different stakeholders will be best placed to lead on the many different aspects identified within the Recommendations. The Royal Pharmaceutical Society has identified the areas it believes it is best placed

to lead on and has committed to take these items forward. To address other themes within the Recommendations, the Royal Pharmaceutical Society will encourage other stakeholders to take the lead supported by the Royal Pharmaceutical Society.

Developing an implementation plan to meet these targets will require determining what work needs to be undertaken, identifying key stakeholders who wish to work collaboratively on Royal Pharmaceutical Society led themes, identify stakeholders who may lead on other themes, as well as defining outcomes that will

reliably measure the impact of the work. There will obviously be a need for regular review of progress against the Recommendations and targets set as well as periodic review of any implementation plan to react to changes and developments.

RECOMMENDATION I – ENSURING THE SAFE USE OF MEDICINES

PROMOTE FURTHER RESEARCH INTO THE CAUSES OF MEDICATION ERRORS IN PATIENTS AND RESEARCH INTO INTERVENTIONS TO REDUCE THOSE ERRORS

- **Stakeholders**
Schools of Pharmacy, NHS (particularly those involved in the prescribing and supply of medicines; assessing medicines data in Scotland), Regulatory Agencies, National Institute for Health and Care Excellence/ Scottish Medicines Consortium, Pharmaceutical Industry, Research Charities (including pharmacy charities e.g. Pharmacy Research UK; disease charities e.g. Arthritis Research UK), Pharmacy Groups and Organisations, Medical Royal Colleges (such as the Royal College of General Practitioners), Patients and the Public.
- **Action Plan**
Establish the current evidence base within pharmacy pertaining to the safe use of medicines; develop robust evidence that demonstrates the impact of pharmacy interventions in the safe use of medicine; and work with research charities to stimulate work into how medicines can be used more safely.
- **Time Scale**
Short term – review evidence and approach stakeholders who may be interested in collaboration.
Medium term – begin to see improvements in the impact of pharmacist-led interventions in some areas of the profession between 2-5 years.

IMPROVE PATIENT UNDERSTANDING OF THE RISKS AND BENEFITS OF THEIR MEDICATION

- **Stakeholders**
Schools of Pharmacy, NHS (particularly those involved in the prescribing and supply of medicines; assessing medicines data in Scotland), Regulatory Agencies, National Institute for Health and Care Excellence/ Scottish Medicines Consortium, Pharmaceutical Industry, Research Charities (including pharmacy charities

e.g. Pharmacy Research UK; disease charities e.g. Arthritis Research UK), Pharmacy Groups and Organisations, Medical Royal Colleges (such as the Royal College of General Practitioners), Patients and the Public.

- **Action Plan**
Inform patients and the public that no medicine is completely safe and that all medicines are associated with risks and benefits; encourage discussion about the risks and benefits of newly marketed medicines with patients; support interventions that may avoid the need for medicine taking.
- **Time Scale**
Medium term – Implement awareness strategies to improve the understanding of the public to the risks and benefits of taking new medicines within 2-5 years.

IMPROVE PHARMACOVIGILANCE AND REPORTING OF SUSPECTED ADVERSE DRUG REACTIONS BY HEALTHCARE PROFESSIONALS AND PATIENTS TO IDENTIFY ANY SAFETY ISSUES FOLLOWING THE LAUNCH OF A MEDICINE

- **Stakeholders**
NHS, NICE/SMC/AWSMG, Regulatory Authorities, Government Health Departments, Pharmaceutical Industry, Pharmacists, other Healthcare Professionals, Public and Patients.
- **Action Plan**
Determine strategies that will improve reporting of adverse events to medicines and communicate to the necessary group including healthcare professionals, the public and patients.
- **Time Scale**
Short term – Approach stakeholders who may be interested in leading and collaborating on this Recommendation.
Medium term – Begin to see improvements in reporting of adverse drug reactions.

ENCOURAGE DEVELOPMENTS IN TOXICOLOGY TESTING, PREDICTIVE PHARMACOKINETICS, DRUG DELIVERY, CLINICAL TRIAL DESIGN AND AGE-RELATED FORMULATIONS TO AID THE DEVELOPMENT OF SAFER MEDICINES

- **Stakeholders**
NHS, Pharmaceutical Industry, Regulatory Authorities, Academia, Pharmaceutical Scientist Organisations, Healthcare Professionals.
- **Action Plan**
Encourage stakeholders to determine more efficient means to identify the toxicity of new drugs and formulations and better methods to assess the toxicity of drugs and medicines.

- **Time Scale**
Short term – Facilitate collaboration between stakeholders within the first 12 months.
Medium term – Facilitate knowledge transfer and partnership in the development of toxicology testing, predictive pharmacokinetics, drug delivery, clinical trial design and age-related formulations.
Long term – Begin to see improvements in the methodology of toxicity testing, predictive pharmacokinetics, drug delivery, clinical trial design and age-related formulations.

RECOMMENDATION 2 – IMPROVING ANTIMICROBIAL STEWARDSHIP AND STIMULATING NEW ANTIMICROBIAL DEVELOPMENT

EDUCATE THE PUBLIC AND PATIENTS ON THE USE OF ANTIMICROBIALS AND THEIR PLACE IN THERAPY

- **Stakeholders**
Schools of Pharmacy, NHS (especially Procurement Divisions), Government Health Departments, Pharmaceutical Industry, Industrial Associations (including the Association of British Pharmaceutical Industries; Ethical Medicines Industry Group; European Federation of Pharmaceutical Industries and Associations), Other Health Professions (especially Royal College of Nursing; Royal College of General Practitioners; British Society of Antimicrobial Chemotherapy; Hospital Infection Society), Public, Patient Groups and Organisations.
- **Action Plan**
Develop educational materials for the public and patients; engage in the development of educational materials for pharmacists and allied healthcare professionals and students; and work with patient groups to inform public attitudes towards antimicrobial agents.
- **Time Scale**
Short term – develop educational and support materials for dissemination within 12 months.

ENCOURAGE FURTHER DEVELOPMENT OF ANTIMICROBIAL STEWARDSHIP BY HEALTHCARE PROFESSIONALS TO MAINTAIN THE EFFECTIVENESS OF CURRENT AND ANY FUTURE ANTIMICROBIALS

- **Stakeholders**
Schools of Pharmacy (in educating future pharmacists), NHS (procurement divisions), Government Health Departments, Pharmaceutical Industry (ABPI; Ethical Medicines Industry Group (EMIG); European Federation of Pharmaceutical Industries and Associations (EFPIA)), Other Health Professions (Royal College of Nursing; RCGP; British Society of Antimicrobial Chemotherapy; Hospital Infection Society), Public, Patient Groups and Organisations.
- **Action Plan**
Support evidence-based approaches to antimicrobial stewardship; and develop networks to disseminate best practice in antimicrobial stewardship.
- **Time Scale**
Short term – Investigate the current best practice perspectives on microbial stewardship and encourage dissemination.
Long term – Influence the international community to initiate a global collaboration and joined-up stewardship of antimicrobial use.

SUPPORT THE DISCOVERY AND DEVELOPMENT OF NEW ANTIMICROBIALS OR TREATMENT METHODS, BY DEVELOPING NEW FINANCIAL INCENTIVES

- **Stakeholders**
NHS, NICE/SMC/AWSMG, Government Health Departments, Pharmaceutical Industry, Public and Patients.

- **Action Plan**
Work with stakeholders to ensure research into the discovery of new antimicrobials or treatment methods is financially attractive.
- **Time Scale**
Short term – Arrange meetings of stakeholders who may lead this work with support from the Royal Pharmaceutical Society.

RECOMMENDATION 3 – ADOPTING NEW TECHNOLOGIES

EDUCATE THE PUBLIC AND PATIENTS ABOUT THE ETHICAL AND MORAL ISSUES SURROUNDING THE USE OF NEW TECHNOLOGIES AND MEDICINES SUCH AS GENE THERAPY, REGENERATIVE MEDICINE, THERAPEUTIC VACCINES AND STRATIFIED MEDICINE

- **Stakeholders**
NHS (especially Academic Health and Science Networks; NHS Improving Quality (England)), Government Health Departments (Chief Pharmaceutical Officers), National Institute for Health and Care Excellence/Scottish Medicines Consortium, Regulatory Agencies (Medicines and Healthcare Products Regulatory Agency, European Medicines Agency; Health Research Authority), Pharmaceutical Science Organisations (including the Academy of Pharmaceutical Sciences; UK Controlled Release Society), Other Health Professions (such as Royal College of General Practitioners; Royal College of Physicians; Royal College of Nursing), Public and Patient Groups and Organisations (including the Richmond Group; National Voices and the Patient Information Forum).
- **Action Plan**
Educate the public and patients about the ethical and moral issues surrounding the use of new technologies. Develop literature and other means of communicating with the public and patients that highlights the benefits as well as the ethical and moral issues around the use of new and specialised medicines.
- **Time Scale**
Short term – Begin to produce educational and support material for patients and the public within 12 months.

ENSURE NEW TECHNOLOGIES AND MEDICINES FULFIL THEIR POTENTIAL

- **Stakeholders**
Pharmaceutical Industry, Academia, Regulatory Authorities, Government, Pharmaceutical Science Organisations.
- **Action Plan**
Facilitate an initial meeting to encourage co-operation and collaboration between interested stakeholders.
- **Time Scale**
Short term – Arrange a meeting with relevant stakeholders within 12 months.

ENCOURAGE THE DEVELOPMENT OF APPROPRIATE MODELS OF REIMBURSEMENT TO SUPPORT THE USE AND DEVELOPMENT OF NEW TECHNOLOGIES

- **Stakeholders**
NHS, Pharmaceutical Industry, Government, NICE/SMC/AWSMG.
- **Action Plan**
Facilitate initial discussions with stakeholders to determine new, expensive technologies can be introduced to the satisfaction of all stakeholders. All possible models must be fully investigated, while still allowing for lobbying for changes to ways in which new technologies are funded.
- **Time Scale**
Short term – arrange a meeting of stakeholders to identify who is most suitable to lead this work with support from the Royal Pharmaceutical Society.
Long term – Due to the nature of these changes it may take an extended period of time to implement them.

RECOMMENDATION 4 – SUPPORTING THE DEVELOPMENT OF NEW AND INNOVATIVE MEDICINES

ENCOURAGE THE ADOPTION OF NEW TECHNOLOGIES AND INNOVATIVE APPROACHES THAT ASSIST IN DRUG TARGET IDENTIFICATION, REDUCING DRUG ATTRITION, OPTIMISING MEDICINES DEVELOPMENT AND CLINICAL TRIALS AND IMPROVING THE SAFETY PROFILE OF MEDICINES

- **Stakeholders**
Pharmaceutical and Biotechnology Industries, Academia, Regulatory Authorities, Professional Scientific Bodies (e.g. Royal Society of Chemistry; Society of Biology; British Pharmacological Society), Pharmacy and Pharmaceutical Science Organisations.
- **Action Plan**
Support relevant stakeholders to identify new technologies and develop a plan as to how they may be successfully incorporated within marketing authorisation applications.
- **Time Scale**
Short term – Identify new technologies needing support and develop a strategy to aid stakeholders.

FACILITATE THE SUPPLY OF NEW AND INNOVATIVE MEDICINES, BY REDUCING THE COST AND TIME TO BRING THESE MEDICINES TO THE MARKET

- **Stakeholders**
Pharmaceutical and Biotechnology Industries, Academia, Regulatory Authorities, Government, Professional Scientific Bodies (e.g. Royal Society of Chemistry; Society of Biology; British Pharmacological Society), NHS, Public and Patients.
- **Action Plan**
Identify stakeholders most suitable to lead the work and support discussions between interested parties to facilitate the goal.
- **Time Scale**
Short term – arrange a meeting of stakeholders to identify who is most suitable to lead this work with support from the Royal Pharmaceutical Society.

STREAMLINE AND REDUCE THE REGULATORY BURDEN ASSOCIATED WITH APPROVAL, PARTICULARLY OF NEW AND INNOVATIVE MEDICINES, WHILE CONTINUING TO ENSURE PATIENT SAFETY

- **Stakeholders**
Regulatory Authorities, Pharmaceutical and Biotechnology Industries, Academia, the Public and Patients
- **Action Plan**
Arrange a meeting of interested parties to identify the stakeholder most suitable to lead the work and to enable discussions aimed at facilitating the goal.
- **Time Scale**
Short term – Initiate and co-ordinate a meeting of stakeholders within 12 months.

ENCOURAGE PARTICIPATION AND TRANSPARENCY IN CLINICAL TRIALS

- **Stakeholders**
Regulatory Authorities, Pharmaceutical and Biotechnology Industries, Academia, the Public and Patients.
- **Action Plan**
Arrange a meeting of interested parties to identify the stakeholder most suitable to lead the work and to enable discussions aimed at facilitating the goal.
- **Time Scale**
Short term – Initiate and co-ordinate a meeting of stakeholders within 12 months.

RECOMMENDATION 5 – INCREASING THE EVIDENCE BASE FOR PHARMACY

INCREASE THE HEALTH SERVICES RESEARCH EXPERTISE WITHIN THE PROFESSION

- **Stakeholders**
Schools of Pharmacy, Pharmacy and Pharmaceutical Scientists Profession, Other Health Professions, Royal Pharmaceutical Faculty, Patients and Public, NHS, Government Health Departments, Research Funding Bodies.
- **Action Plan**
Increase the proportion of the pharmacy profession that is research active and celebrate the achievements of pharmacists undertaking research in their specialist area.
- **Time Scale**
Short term – Encourage co-operation and collaboration of academia and practitioners of pharmacy within the first 12 months in some areas.

DEMONSTRATE THE CLINICAL AND COST EFFECTIVENESS OF NHS PHARMACY SERVICES BY MEANS OF WELL-CONDUCTED, DEFINITIVE TRIALS THAT ARE APPROPRIATELY FUNDED TO ENHANCE THE ROLE OF PHARMACY IN THE TREATMENT OF PATIENTS

- **Stakeholders**
Schools of Pharmacy and other Higher Education Institutions (HEIs), Pharmacy Profession, Pharmacy

Organisations, other Health Professions, Pharmacy Postgraduate Education Bodies, Pharmacy Employers, Government Health Departments, NHS (including NHS Commissioning Groups) and Social Care organisations, Royal Pharmaceutical Society Faculty, Organisations representing Patients and the Public, Research Funding Bodies.

- **Action Plan**
Ensure all evidence is disseminated as widely as possible, in a range of styles tailored to different audiences, especially peer-reviewed reports of substantive studies; and to address the paucity of evidence in some aspects of pharmacy, well-conducted, definitive trials assessing the clinical and cost effectiveness of NHS pharmacy roles should be funded and conducted.
- **Time Scale**
Short term – Investigate the current best practice and evidence on pharmacist-led care of patients and facilitate dissemination.
Medium term – Begin to see initial improvements in the evidence base of best practice. Encourage changes in student pharmacist education to ensure that best practice is integrated into all educational programmes. Facilitate further research into best practice approaches and pharmacist-led interventions.

RECOMMENDATION 6 – SUPPORTING PHARMACEUTICAL SCIENCE IN THE UK

ENCOURAGE INVESTMENT IN SCIENTIFIC EDUCATION AND TRAINING TO ENSURE A HIGHLY SKILLED AND ADAPTIVE PHARMACEUTICAL SCIENCE WORKFORCE

- **Stakeholders**
Government, NHS, Pharmaceutical Industry, Academia, Pharmaceutical Science Stakeholders/Organisations, Higher Education Funding Councils in England, Scotland and Wales.

- **Action Plan**
Identify interested stakeholders and determine the education and training needs of the 16+ workforce and lobby funders of education and training to encourage funds to be made available in the workplace.
- **Time Scale**
Short term – Identify interested stakeholders and facilitate initial meeting within 12 months.

ENSURE THAT THE UK REMAINS A MAJOR PLAYER IN THE DEVELOPMENT OF NEW AND INNOVATIVE MEDICINES BY EXPANDING CURRENT GOVERNMENT INITIATIVES AIMED AT MAKING THE UK AN ATTRACTIVE LOCATION FOR COMPANIES OF ALL SIZES

- **Stakeholders**
Government, Pharmaceutical Industry, Academia, NHS, Pharmacy and Pharmaceutical Scientist Organisations.
- **Action Plan**
Contribute to work being led by other stakeholders in lobbying Government to expand current initiatives and develop new ones.
- **Time Scale**
Short term – Arrange a meeting of interested stakeholders within 18 months.

INCREASE SUPPORT FOR MORE ACADEMIC/NHS/ INDUSTRIAL PARTNERSHIPS

- **Stakeholders**
Pharmaceutical and Biotechnology Industries, Academia, NHS, the Public and Patients.
- **Action Plan**
Arrange a meeting of interested parties to identify the stakeholder most suitable to lead the work and to enable discussions aimed at facilitating the goal.
- **Time Scale**
Short term – Initiate and co-ordinate a meeting of stakeholders within 12 months.

RECOMMENDATION 7 – IMPROVING ACCESS TO MEDICINES AT A GLOBAL LEVEL

TACKLE DISEASE IN DEVELOPING COUNTRIES AND ENSURE THE EQUITABLE ACCESS OF QUALITY MEDICINES TO ALL PATIENTS

- **Stakeholders**
Pharmaceutical Industry, Global Organisations (e.g. WHO, UNICEF, FIP), Governments, National, Multinational and International Pharmacy and Pharmaceutical Science Professional Bodies, other Healthcare Professions, Public and Patients.
- **Action Plan**
Contribute to the work of international (FIP) and Multinational (Commonwealth) pharmacy groups to influence international organisations such as the WHO to progress the goal.
- **Time Scale**
Long term – Due to the nature of these changes it may take an extended period of time to implement these changes.

SUPPORT THE RESPONSIBLE RE-USE OF MEDICINES TO IMPROVE ACCESS TO MEDICINES IN DEVELOPING WORLD COMMUNITIES, THEREBY IMPROVING HEALTH

- **Stakeholders**
Pharmaceutical Industry, Governments, Global Organisations (e.g. WHO, UNICEF), Charities, International Pharmacy and Pharmaceutical Science Professional Bodies, Pharmacy Professional Bodies, other Healthcare Professions, Public and Patients.
- **Action Plan**
Determine legal and responsible means of enabling the pharmacy community in Great Britain to provide useful donations of medicines to other countries in which there is a shortage and a need.
- **Time Scale**
Medium term – Clarify the legal position surrounding medicines donations and identify other hurdles that must be overcome within 2-5 years.

Long term – Facilitate the donations of medicines to other countries in which there is a shortage and a need.

PREVENT HARM TO PATIENTS BY THE REMOVAL OF FALSIFIED AND COUNTERFEIT MEDICINES FROM THE LEGITIMATE MEDICINES SUPPLY CHAIN AND ILLEGAL SUPPLY THROUGH THE INTERNET

- **Stakeholders**
National, Multinational and International Pharmacy and Pharmaceutical Science Professional Bodies, Regulatory Authorities, Governments, Pharmaceutical Industry, Public and Patients.
- **Action Plan**
Contribute to the work of national, multinational and international organisations and agencies to address the problems associated with falsified and counterfeit medicines and internet sales of medicines.
- **Time Scale**
Long term – Due to the nature of these changes it may take an extended period of time to implement them.

6. REFERENCES

1. Li-Wan-Po, A. Pharmacogenetics and personalised medicine (editorial). *Journal of Clinical Pharmacy and Therapeutics* (2012) **37** 617–619.
2. Personalised medicines: Hopes and realities. The Royal Society, London (2005). (http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/publications/2005/9631.pdf – accessed 9 October 2013).
3. Personalised medicine. Postnote Number 329. Parliamentary Office of Science and Technology, London (2009). (<http://www.parliament.uk/documents/post/postpn329.pdf> – accessed 9 October 2013).
4. Traynor, K. FDA approves first stem-cell therapy. *American Journal of Health-System Pharmacy* (2011) **68** 2316.
5. Ptaszek, L.M. et al. Stem cells 1 – Towards regenerative therapy for cardiac disease. *Lancet* (2012) **379** 933–942.
6. Badylak, S.F. et al. Stem cells 2 – Engineered whole organs and complex tissues. *Lancet* (2012) **379** 943–952.
7. Badylak, S.F. and Nerem, R.M. Progress in tissue engineering and regenerative medicine. *Proceedings of the National Academy of Science* (2010) **107** 3285–3286.
8. APBI. Developing new medicines. (<http://www.abpi.org.uk/industry-info/new-medicines/Pages/default.aspx> – accessed 4 April 2014).
9. DiMasi, J.A. et al. Trends in risks associated with new drug development: success rates for investigational drugs. *Clinical Pharmacology and Therapeutics* (2010) **87** 272–277.
10. Suntharalingam, G. et al. Cytokine storm in a phase I trial of the anti-CD28 monoclonal antibody TGN1412. *New England Journal of Medicine* (2006) **355** 1018–1028.
11. Pirmohamed, M. et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18,820 patients. *British Medical Journal* (2004) **329** 15–19.
12. Making the safety of patients everyone's highest priority. Patients Safety First, London (2013) (<http://www.patientsafetyfirst.nhs.uk/content.aspx?path=/> – accessed 9 October 2013).
13. 1000 Lives Plus. NHS Wales, Cardiff (2013). (<http://www.wales.nhs.uk/sites3/home.cfm?orgid=781> – accessed 9 October 2013).
14. Scottish Patient Safety Programme. NHS Scotland and Healthcare Improvement Scotland (2013). (<http://www.scottishpatientsafetyprogramme.scot.nhs.uk/programme> – accessed 9 October 2013).
15. Safer Ambulatory Syringe Drivers. NHS England, London (2010). (<http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=92908&q=0%c2%acsyringe+driver%c2%ac> – accessed 9 October 2013).
16. Franklin, B.D. et al. An evaluation of two automated dispensing machines in UK hospital pharmacy. *International Journal of Pharmacy Practice* (2008) **16** 47–53.
17. Keeping patients safe when they transfer between care providers – getting the medicines right. Royal Pharmaceutical Society, London (2012). (<http://www.rpharms.com/current-campaigns-pdfs/Royal-Pharmaceutical-Society-transfer-of-care-final-report.pdf> – accessed 30 September 2013).
18. Barrett, N.A. et al. Management of long-term hypothyroidism: a potential marker of quality of medicines reconciliation in the intensive care unit. *International Journal of Pharmacy Practice* (2012) **20** 303–306.
19. Medicines Reconciliation: A Guide to Implementation. NHS National Prescribing Centre, Liverpool (2008). (http://www.npc.nhs.uk/improving_safety/medicines_reconciliation/resources/reconciliation_guide.pdf – accessed 9 October 2013).
20. Office for National Statistics. Business Enterprise Research and Development (2011). *Statistical Bulletin* (2012). (http://www.ons.gov.uk/ons/dcp171778_287868.pdf – accessed 4 April 2014).
21. ONS Annual Business Survey 2009 Provisional Results – Sections C: Manufacturing. Office of National Statistics, Newport. (Release Date 16 November 2010).

22. Statistical bulletin: UK Business Enterprise Research and Development, 2009. Office of National Statistics, Newport (2010). (<http://www.ons.gov.uk/ons/rel/rditl/bus-ent-res-and-dev/2009-edition/index.html> – accessed 9 October 2013).
23. New Academic Health Science Networks announced. NHS England, London (2013). (<http://www.england.nhs.uk/2013/05/23/acc-health-sci-ntwrk/> – accessed 2 October 2013).
24. Skills needs for biomedical research – creating the pools of talent to win the innovation race. ABPI, London (2008). (<http://www.abpi.org.uk/our-work/library/industry/Documents/skills-biomedical-research.pdf> – accessed 9 October 2013).
25. Koehn, F.E. and Carter, G.T. <http://www.nature.com/nrd/journal/v4/n3/abs/nrd1657.html> – al The evolving role of natural products in drug discovery. *Nature Reviews Drug Discovery* (2005) **4** 206–220.
26. Thomas, T.R.A. et al. Marine drugs from sponge-microbe association – a review. *Marine Drugs* (2010) **8** 1417–1468.
27. Cho, Y. et al. From snake venom toxins to therapeutics – cardiovascular examples. *Toxicon* (2012) **59** 497–506.
28. Jiongyu, L. et al. Antimicrobial peptides from the skin of the Asian frog, *Odorrana jingdongensis*: de novo sequencing and analysis of tandem mass spectrometry data. *Journal of Proteomics* (2012) **75** 5807–5821.
29. Posner, B.A. High-throughput screening-driven lead discovery: meeting the challenges of finding new therapeutics. *Current Opinion in Drug Discovery and Development* (2005) **8** 487–494.
30. Martin, E.M. et al. Protein kinase inhibitors: insights into drug design from structure. *Science* (2004) **303** 1800–1805.
31. Murray, C.W. and Rees, D.C. The rise of fragment-based drug discovery. *Nature Chemistry* (2009) **1** 187–192.
32. Cho, C.R. et al. The application of systems biology to drug discovery. *Current Opinion in Chemical Biology* (2006) **10** 294–302.
33. Hu, F.B. Globalization of Diabetes – The role of diet, lifestyle, and genes. *Diabetes Care* (2011) **34** 1249–1257.
34. Mellstedt, H. et al. The challenge of biosimilars. *Annals of Oncology* (2008) **19** 411–419.
35. Crommelin, D. et al. Pharmaceutical evaluation of biosimilars: important differences from generic low-molecular-weight pharmaceuticals. *The European Journal of Hospital Pharmacy Science* (2005) **11** 11–17.
36. Roger, S.D. Biosimilars: current status and future directions. *Expert Opinion on Biological Therapy* (2010) **10** 1011–1018.
37. Doherty, T.M. New vaccines against tuberculosis. *Tropical Medicine and International Health* (2004) **9** 818–826.
38. Lambert, P.H. et al. New vaccines against tuberculosis. *Clinics in Chest Medicine* (2009) **30** 811–826.
39. FDA approves first cord blood product (press release). US Food and Drug Administration, Silver Spring (2011). (www.fda.gov/newsevents/newsroom/pressannouncements/ucm279575.html – accessed 1 October 2013).
40. Sipp, D. and Turner, L. US regulation of stem cells as medical products. *Science* (2012) **338** 1296–1297.
41. Jing, W. et al. Metformin activates an atypical PKC-CBP pathway to promote neurogenesis and enhance spatial memory formation. *Cell Stem Cell* (2012) **11** 23–35.
42. Spellberg, B. et al. The future of antibiotics and resistance. *New England Journal of Medicine* (2013) **368** 299–302.
43. Davies, S.C. Annual report of the chief medical officer Volume Two, 2011 Infections and the rise of antimicrobial resistance. Department of Health, London (2013). (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/138331/CMO_Annual_Report_Volume_2_2011.pdf accessed 1 October 2013) – accessed 9 October 2013).
44. Clardy, J. et al. New antibiotics from bacterial natural products. *Nature Biotechnology* (2006) **24** 1541–1550.
45. Coates, A.R.M. and Hu, Y. Novel approaches to developing new antibiotics for bacterial infections. *British Journal of Pharmacology* (2007) **152** 1147–1154.

46. Reynolds G. P. et al. Pharmacogenomics in psychiatry: the relevance of receptor and transporter polymorphisms. *British Journal of Clinical Pharmacology* (2013) **77** 654–672.
47. Nohaile, M. The biomarker is not the end. *Drug Discovery Today* (2011) **16** 878–883.
48. McClellan, K.A. Personalized medicine and access to health care: potential for inequitable access? *European Journal of Human Genetics* (2013) **21** 143–147.
49. Kearns, G. et al. Developmental pharmacology – Drug disposition, action and therapy in infants and children. *New England Journal of Medicine* (2003) **349** 1157–1167.
50. Routledge, P. Pharmacokinetics in children. *Journal of Antimicrobial Chemotherapy* (1994) **34** (suppl A) 19–24.
51. Medicines for Children – Background. MHRA, London. (www.mhra.gov.uk/Howweregulate/Medicines/Medicinesforchildren/#12 – accessed 4 April 2014).
52. Tomlin, S. Understanding how to select appropriate liquid medicines for children will ensure they receive the best-available product for their needs. *Pharmacy in Practice* (2007) **17** 211–214.
53. Mossialos, E et al. Expanding the role of community pharmacists: Policymaking in the absence of policy-relevant evidence? *Health Policy* (2013) **111** 135–148.
54. Pharmacy in England: Building on strengths – Delivering the future. Department of Health, White Paper. London (April 2008). (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/228858/7341.pdf – accessed 4 April 2014).
55. Technical patient safety solutions for medicines reconciliation on admission of adults to hospital. National Institute for Health and Clinical Excellence and National Patient Safety Agency (December 2007). (<http://www.nice.org.uk/nicemedia/live/11897/38560/38560.pdf> – accessed 10 July 2012).
56. Campbell, G. et al. Clinical pharmacy services in a London hospital, have they changed? *International Journal of Clinical Pharmacology* (2013) **35** 688–691.
57. Country profiles on nutrition, physical activity and obesity in the 53 WHO European Region Member States. Methodology and summary World Health Organisation (2013). (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/publications/2013/country-profiles-on-nutrition,-physical-activity-and-obesity-in-the-53-who-european-region-member-states.-methodology-and-summary> – accessed 13 March 2014).
58. Janson, B. and Thursky, K. Dosing of antibiotics in obesity. *Current Opinion in Infectious Diseases* (2012) **25** 634–649.
59. Department of Health: Prescribing costs in primary care – Second Report of Session 2007–08 (2007) London. (2010) (<http://www.publications.parliament.uk/pa/cm200708/cmselect/cmpubacc/173/173.pdf> – accessed 3 March 2014).
60. Hepler, C.D. and Strand, L.M. Opportunities and responsibilities in pharmaceutical care. *American Journal of Hospital Pharmacy* (1990) **47** 533–543.
61. Prescription for Excellence – A Vision and Action Plan for the right pharmaceutical care through integrated partnerships and innovation. Scottish Government, Edinburgh (September 2013). (<http://www.scotland.gov.uk/Resource/0043/00434053.pdf> – accessed 1 October 2013).
62. Medicines optimisation: Helping patients to make the most of medicines. Good practice guidance for healthcare professionals in England. Royal Pharmaceutical Society, London (May 2013). <http://www.rpharms.com/promoting-pharmacy-pdfs/helping-patients-make-the-most-of-their-medicines.pdf> – accessed 11 June 2013).
63. American College of Clinical Pharmacy. The definition of clinical pharmacy. *Pharmacotherapy*. (2008) **28** 816–817.
64. Cousins, D. Current status of the monitoring of medication practice. *American Journal of Health-System Pharmacists* (2009) **66** S49–S56.
65. MacLaren, R. and Bond, C.A. Effects of pharmacist participation in intensive care units on clinical and economic outcomes of critically ill patients with thromboembolic or infarction-related events. *Pharmacotherapy* (2009) **29** 761–768.

66. Knibbe, C.A. and Tjoeng, M.M. Clinical pharmacist on intensive care unit saves lives and reduces costs. *Critical Care Medicine* (2008) **36** 3269–3270.
67. McKenzie, C.A. et al. Impact of a specialist pharmacist on prescribing practice in intensive care. *Intensive Care Medicine* (1996) **22** (Suppl 3) S301.
68. McKenzie, C. Personal communication PROTECTED-ICU UK trial.
69. Blenkinsopp, A. et al. Medication reviews. *British Journal Clinical Pharmacology* (2012) **74** 573–580.
70. Hamley, J.H. et al. Integrating clinical pharmacists into the primary health care team: a framework for rational and cost effective prescribing. *Scottish Medical Journal* (1997) **42** 4–7.
71. McIntyre, A.M. et al. New patients presenting to their GP with dyspepsia: does *Helicobacter pylori* eradication minimise the cost of managing these patients? *International Journal of Clinical Practice* (1997) **51** 276–281.
72. Elliott, R. A. et al. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharmacy World and Science* (2008) **30** 17–23.
73. Clifford, S. et al. Patient-centred advice is effective in improving adherence to medicines. *Pharmacy World and Science* (2006) **28** 165–170.
74. Barber, N. et al. Patients' problems with new medication for chronic conditions. *Quality & Safety in Health Care* (2004) **13** 172–175.
75. Nkansah, N. et al. Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. *Cochrane Database of Systematic Reviews* 2010, Issue 7. Art. No.: CD000336. DOI: 10.1002/14651858.CD000336.pub2. [(http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000336.pub2/pdf/standard – accessed 9 October 2013).
76. George, J. et al. Benefits and challenges of prescribing and training implementation: perceptions and early experiences of Royal Pharmaceutical Society GB prescribers. *International Journal of Pharmacy Practice* (2007) **15** 23–30.
77. Bond, C.M. et al. Pharmacist led management of chronic pain in primary care: the experiences of patients, pharmacists and GPs. *International Journal of Pharmacy Practice* (2011) **19** (supp 2) 24–25.
78. Porteous, T. et al. Preferences for self-care or consulting a health professional in minor illness; a discrete choice experiment. *British Journal of General Practice* (2006) **56** 911–917.
79. Paudyal, V. et al. Are pharmacy-based minor ailment schemes a substitute for other service providers? *British Journal of General Practice* (2013) **63** e472–e482.
80. Minor ailment schemes. National Prescribing Centre, Liverpool (2011). (www.npc.nhs.uk/quality/minor/index.php – accessed 9 May 2013).
81. Minor ailment service (MAS). NHS Scotland, Edinburgh. (http://www.communitypharmacy.scot.nhs.uk/core_services/mas.html. – accessed 9 May 2013).
82. Bond, C.M. et al. Community pharmacists' attitudes to the deregulation of medicines and to their extended role. *International Journal of Pharmacy Practice* (1993) **2** 26–30.
83. Ryan, M. and Bond, C.M. Dispensing doctors and prescribing pharmacists. *Pharmacoeconomics* (1994) **5** 8–17.
84. Stead, L.F. et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews* (2008) Issue 1. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub3. (www.thecochranelibrary.com/userfiles/ccoch/file/World%20No%20Tobacco%20Day/CD000146.pdf – accessed 9 October 2013).
85. Watson, M.C. et al. Oral versus intra-vaginal imidazole and triazole anti-fungal agents for the treatment of uncomplicated vulvovaginal candidiasis (thrush): a systematic review. *British Journal of Obstetrics and Gynaecology* (2002) **109** 85–95.
86. Padwal, R.S. et al. Long-term pharmacotherapy for obesity and overweight. *Cochrane Database of Systematic Reviews* (2003), Issue 4. Art. No.: CD004094. DOI: 10.1002/14651858.CD004094.pub2. (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004094.pub2/pdf/standard> – accessed 9 October 2013).
87. Smith, S.M. et al. Over-the-counter (OTC) medications for acute cough in children and adults in ambulatory settings. *Cochrane Database of Systematic Reviews* (2012) Issue 8. Art. No.: CD001831. DOI: 10.1002/14651858.CD001831.pub4. (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001831.pub4/pdf/standard> – accessed 9 October 2013).

88. Ngwerume, K. The development and effect of evidence-based portfolios on the supply of non-prescription medicines [dissertation]. Aberdeen: University of Aberdeen (2010).
89. Watson, M.C. et al. Factors predicting the guideline compliant supply (or non-supply) of non-prescription medicines in the community pharmacy setting. *British Medical Journal* (2006) **15** 53–57.
90. Garner, M. and Watson, M.C. Using linguistic analysis to explore medicine counter assistants' communication during consultations for non-prescription medicines. *Patient Education and Counselling* (2007) **65** 51–57.
91. Watson, M.C. et al. Simulated patient visits with immediate feedback to improve the supply of over-the-counter medicines: A feasibility study. *Family Practitioner* (2009) **26** 532–542.
92. Haynes, R.B. et al. Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews* (2008) Issue 2. Art. No.: CD000011. DOI: 10.1002/14651858.CD000011.pub3. (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000011.pub3/pdf/standard> – accessed 9 October 2013).
93. Costing statement: Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence. NHS National Institute for Health and Clinical Excellence, London (26 January 2009). (<http://www.nice.org.uk/nicemedia/live/11766/42968/42968.pdf> – accessed 26 September 2013.)
94. Adherence to long-term therapies: evidence for action. World Health Organisation, Geneva (2003). (<http://apps.who.int/medicinedocs/pdf/s4883e/s4883e.pdf> – accessed 12 June 2013).
95. Marinker, M. et al. From Compliance to Concordance. Achieving shared goals in medicine taking. The Royal Pharmaceutical Society of Great Britain, London (March 1997).
96. Bond, C. et al. Prescribing and partnership with patients. *British Journal of Clinical Pharmacology* (2012) **74** 581–588.
97. Paterson, D.L. et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine* (2000) **133** 21–30.
98. Horne, R. et al. Concordance, adherence and compliance in medicine taking. Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R & D (NCCSDO). London (2005). (http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf – accessed 12 June 2013).
99. Horne, R. et al. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health* (1999) **14** 1–24.
100. Nunes, V. et al. Clinical guidelines and evidence review for medicines adherence: Involving patients in decisions about prescribed medicines and supporting adherence. National Collaborating Centre for Primary Care and Royal College of General Practitioners, London (2009).
101. Berry, D.C. et al. Provision of information about drug side-effects to patients. *Lancet* (2002) **359** 853–854.
102. Raynor, D.K. The benefits outweigh the risks – who says? *Pharmaceutical Journal* (2013) **290** 616–617.
103. Raynor, D.K. et al. A systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines. *Health Technology Assessment* (2007) **11** 1–178.
104. Always read the leaflet: getting the best information with every medicine. Report of the Committee on Safety of Medicines Working Group on Patient Information. Medicines and Healthcare Products Regulatory Agency. The Stationery Office London (2005). (<http://www.mhra.gov.uk/home/groups/pl-a/documents/publication/con2018041.pdf> – accessed 12 June 2013).
105. Raynor, D.K. Addressing medication literacy: a pharmacy practice priority. *International Journal of Pharmacy Practice* (2009) **17** 257–259.
106. Raynor, D.K. Health literacy – is it time to shift our focus from patient to provider? *British Medical Journal* (2012) **344** e2188.
107. Staples, B. and Bravender, T. Drug compliance in adolescents: Assessing and managing modifiable risk factors. *Paediatric Drugs* (2002) **4** 503–513.

108. Gray, N.J. et al. Arthriting: Exploring the relationship between identity and medicines use, and to identify the contribution of medicines and pharmacy services, for the care of young people with arthritis. Final report. Pharmacy Research UK, London (2013).
109. Smith, F. and Gray, N. Empowering young patients with long-term conditions to take control of their medicines. *Expert Review of Clinical Pharmacology* (2009) **2** 453–459.
110. Newbould, J. et al. 'I'm fine doing it on my own': partnerships between young people and their parents in the management of medication for asthma and diabetes. *Journal of Child Health Care* (2008) **12** 116–128.
111. Elliott, R.A. et al. Talking about medicines (TABS): involving children and young people with chronic illness in managing their medicines. Final report. NIHR Service Delivery and Organisation programme. Southampton (2013). (http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1704-212_V07.pdf – accessed 12 June 2013).
112. Improving practice and reducing risk in the provision of parenteral nutrition for neonates and children. A report from the paediatric chief pharmacists group. (2011). (www.nppg.scot.nhs.uk/Minimising%20risk%20in%20PN%20for%20children.pdf – accessed 12 June 2013).
113. Ahmed, U. et al. Dosing of oral penicillins in children: is big child=half an adult, small child=half a big child, baby=half a small child still the best we can do? *British Medical Journal* (2011) **343** d7803.
114. Patterson, S.M. et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews* (2012) Issue 5. Art. No.: CD008165. DOI: 10.1002/14651858.CD008165.pub2. (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008165.pub2/pdf/standard> – accessed 10 October 2013).
115. Polypharmacy Guidance. NHS Scotland/Scottish Government, Edinburgh (October 2012). (<http://www.central.knowledge.scot.nhs.uk/upload/Polypharmacy%20full%20guidance%20v2.pdf> – accessed 18 April 2013).
116. Chen, Y-F. et al. Self-reported medication use for older people in England and Wales. *Journal of Clinical Pharmacy and Therapeutics* (2001) **26** 129–140.
117. Claxton, A.J. et al. A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics* (2001) **23** 1296–1310.
118. Stegeman, S. et al. Geriatric drug therapy: neglecting the inevitable majority. *Ageing Research Reviews* (2010) **9** 384–398.
119. Aronson, J.K. In defence of polypharmacy. *British Journal of Clinical Pharmacology* (2004) **57** 119–120.
120. Alldred, D.P. et al. Care Home Use of Medicines Study (CHUMS). Medication errors in nursing and residential care homes – prevalence, consequence, causes and solutions. Report to the Patient Safety Research Portfolio. Department of Health, London (2009). (<http://www.birmingham.ac.uk/Documents/collegemds/haps/projects/cfhcp/psrp/finalreports/PS025CHUMS-FinalReportwithappendices.pdf> – accessed 19 April 2013).
121. Lapane, K.L. et al. Pharmacotherapy interventions undertaken by pharmacists in the Fleetwood phase III study: the role of process control. *Annals of Pharmacotherapy* (2006) **40** 1522–1526.
122. Rathod, S. et al. Cognitive-behavioral therapy for medication-resistant schizophrenia: A review. *Journal of Psychiatric Practice* (2008) **14** 22–33.
123. Honigfeld G. et al. Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine. *Archives of General Psychiatry*. (1988) **45** 789–796.
124. Taylor, D. et al. Editors. *The Maudsley Prescribing Guidelines in Psychiatry*, 11th ed. Wiley-Blackwell, Oxford (2012).
125. HIV in the United Kingdom: 2011 report. Health Protection Agency, London (2011). (http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317131685847 – accessed 10 October 2013).
126. May, M. et al. Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study. *British Medical Journal* (2011) **343** d61016.

127. The renal team – A multi-professional renal workforce plan for adults and children with renal disease. Recommendations of the national renal workforce planning group 2002. British Renal Society, Woking (2002). (http://www.britishrenal.org/getattachment/Workforce-Planning/WFP_Renal_Book1.pdf.aspx – accessed 10 October 2013).
128. Wilson, H. and Barber, N. Review of NHS pharmaceutical care of patients in the community in Scotland. Scottish Government, Edinburgh (August 2013). (<http://www.scotland.gov.uk/Resource/0043/00430209.pdf> – accessed 1 October 2013).
129. Sinclair, H.K. et al. Community pharmacy personnel interventions for smoking cessation. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD003698. DOI: 10.1002/14651858.CD003698.pub2. (<http://www.ncsct.co.uk/usr/pub/community-pharmacy-personnel-interventions.pdf> – accessed 10 October 2013).
130. NHS Smoking Cessation Service Statistics (Scotland) 1st January to 31st December 2011. NHS Scotland (2012). (http://www.scotpho.org.uk/downloads/scotphoreports/scotpho120529_smoking_cessationstatistics2011.pdf – accessed 4 October 2013).
131. Anderson, C. and Blenkinsopp, A. Community pharmacy supply of emergency hormonal contraception: a structured literature review of international evidence. *Human Reproduction* (2006) **21** 272–284.
132. Costelloe, C. et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *British Medical Journal* (2010) **340** c2096.
133. Huttner et al. Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum. *Antimicrobial Resistance and Infection Control* 2013, 2:31.
134. Chapman, A.L.N. et al. Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement. *Journal of Antimicrobial Chemotherapy* (2012) doi:10.1093/jac/dks003 (<http://jac.oxfordjournals.org/content/early/2012/01/31/jac.dks003.full.pdf?keytype=ref&ijkey=E58nX8zVA10cz7P> – accessed 10 October 2013).
135. Little, P et al. Open randomised trial of prescribing strategies in managing sore throat. *British Medical Journal* (1997) **314** 722–727.
136. Dellit T.H et al. IDSA Guidelines. *Clinical infectious diseases*. (2007) **44** 159–177. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub3. (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003543.pub3/pdf/standard> – accessed 10 October 2013).
137. Gerding, D.N. The search for good antimicrobial stewardship. *Joint Commission Journal on Quality Improvement* (2001) **27** 403–404.
138. Tamma, P.D. and Cosgrove, S.E. Antimicrobial stewardship. *Infectious Disease Clinics of North America* (2011) **25** 245–260.
139. Mattick, R.P. et al. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database of Systematic Reviews (2009), Issue 3. Art.No.: CD002209. DOI: 10.1002/14651858.CD002209.pub2. (onlinelibrary.wiley.com/doi/10.1002/14651858.CD002209.pub2/pdf/standard – accessed 10 October 2013).
140. Methadone and buprenorphine for the management of opioid dependence. NICE Technology Appraisal Guidance 114. National Institute for Health and Clinical Excellence, London (2007). (<http://www.nice.org.uk/nicemedia/live/11606/33833/33833.pdf> – accessed 12 June 2013).
141. Simoons, S. et al. The effectiveness of community maintenance with methadone or buprenorphine for treating opiate dependence. *British Journal of General Practice* (2005) **55** 139–146.
142. Woodak, A. and Cooney, A. Effectiveness of sterile needle and syringe programming in reducing HIV/AIDS among injecting drug users. World Health Organisation, Geneva (2004). (http://www.who.int/hiv/pub/prev_care/effectivenesssterileneedle.pdf – accessed 12 June 2013).
143. Jaffray, M. et al. Does training in motivational interviewing for community pharmacists improve outcomes for methadone patients? A cluster randomised controlled trial. *International Journal of Pharmacy Practice* (2013) doi: 10.1111/ijpp.12049.

144. Matheson, C. et al. Community pharmacy services for drug misusers in Scotland: Measuring national service delivery and the development of professional attitudes over a decade. *Journal of Public Health* (2007) **29** 350–357.
145. Matheson, C. et al. A follow up survey of general practice input in drug misuse management. *British Journal of General Practice* (2010) **60** 517–520.
146. Pharmacist-provided immunization compensation and recognition: White paper summarizing APhA/AMCP stakeholder meeting. *Journal of the American Pharmacists Association* (2011) **51** 704–712.
147. Hind, C.A. et al. Successful provision of influenza vaccine from a community pharmacy in Aberdeen. *Pharmaceutical Journal* (2004) **273** 194–196.
148. Warner, J. G. et al. Increasing seasonal influenza vaccination uptake using community pharmacies: experience from the Isle of Wight, England. *International Journal of Pharmacy Practice* (2013) doi: 10.1111/ijpp.12037.
149. Hind, C.A. et al. Needs assessment study for community pharmacy travel medicine services. *Journal of Travel Medicine* (2008) **15** 328–334.
150. Hind, C.A. et al. Travel medicine services from community pharmacy: evaluation of a pilot service. *Pharmaceutical Journal* (2008) **28** 625–628.
151. Wu, T-Y. et al. Ten-year trends in hospital admissions for adverse drug reactions in England 1999–2009. *Journal of the Royal Society of Medicine* (2010) **103** 239–250.
152. Ryan, et al. Prevalence and Causes of Prescribing Errors: The Prescribing Outcomes for Trainee doctors Engaged in Clinical Training (PROTECT) study. *PLOS ONE*. (2014) **9** e79802
153. Avery, A.J. et al. Evaluation of patient reporting of adverse drug reactions to the UK 'Yellow Card Scheme': literature review, descriptive and qualitative analyses, and questionnaire surveys. *Health Technology Assessment* (2011) **15** 1–234.
154. Hopf, Y. et al. Views of healthcare professionals to linkage of routinely collected healthcare data: a systematic literature review. *Journal of the American Medical Informatics Association* (2013) **1**.
155. Keep Well. NHS Health Scotland, Edinburgh (2006). (<http://www.healthscotland.com/keep-well.aspx> – accessed 19 September 2013).
156. Evaluation of the Healthy Living Pharmacy Pathfinder Work Programme 2011–2012. (April 2013) (<http://psnc.org.uk/wp-content/uploads/2013/08/HLP-evaluation.pdf> – accessed 23 April 2013).
157. Making new medicines available. Health Impact Fund. (<http://healthimpactfund.com/> – accessed 1 June 2013).
158. Malaria Fact Sheet No 94. World Health Organisation, Geneva (March 2013). (<http://www.who.int/mediacentre/factsheets/fs094/en/> – accessed 30 September 2013).
159. Tuberculosis Fact Sheet No 104. World Health Organisation, Geneva (February 2013). (<http://www.who.int/mediacentre/factsheets/fs104/en/> – accessed 30 September 2013).
160. Global HIV/AIDS response – Epidemic update and health sector progress towards universal access. Progress Report 2011. WHO, UNICEF and UNAIDS. (2011) (http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20111130_ua_report_en.pdf – accessed 10 October 2013).
161. Number of Deaths due to HIV/AIDS. World Health Organisation, Geneva (2013). (http://www.who.int/gho/hiv/epidemic_status/deaths_text/en/index.html – accessed 30 September 2013).
162. Grace, D. et al. The multiple burdens of zoonotic disease and an ecohealth approach to their assessment. *Tropical Animal Health and Production* (2012) **44** (Suppl 1) S67–S73.
163. Counterfeit Medicines. MHRA, London (2012). (www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/counterfeitmedicinesanddevices/Falsifiedmedicines/index.htm – accessed 15 July 2013).
164. Costello, A. et al. Managing the health effects of climate change. *Lancet* (2009) **373** 1693–1733.
165. Liu, L. et al. Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* (2012) **379** 2151–61.
166. Alexander, A. Pharmacists still have time to help mitigate the effects of climate change. *Pharmaceutical Journal* (2012) **289** 406.

167. Arzymanow B and Manning J Value-based pricing: the wrong medicine for the nation? *2020 health* (2013).
168. A new pathway for the regulation and governance of health research. Academy of Medical Sciences Report (2011).
169. Bond, C.M. et al. Repeat prescribing: An evaluation of the role of community pharmacists in controlling and monitoring repeat prescribing. *British Journal of General Practice* (2000) **50** 271–275.
170. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf – accessed 1 March 2014).
171. Hassell K and Seston EM. *Setting the Research Agenda: The Pharmacy Workforce*. Royal Pharmaceutical Society of Great Britain, London (2001).
172. Hassell, K and Shann, P. *GB Pharmacists work patterns: Summary of the 2002 Pharmacy Workforce Census*. Royal Pharmaceutical Society of Great Britain, London (2003).
173. Guest, D. et al. *Future pharmacy workforce requirements; Workforce modelling and policy recommendations*. Royal Pharmaceutical Society of Great Britain, London (2005).
174. Hassell, K. et al. Contemporary workforce patterns and historical trends: the Pharmacy labour market over the past 40 years. *Pharmaceutical Journal* (2002) **269** 291–296.
175. Hassell, K. et al. The UK pharmacy degree: Attrition rates and demographics of non-completers. *Pharmacy Education* (2007) **7** 249–256.
176. Willis, S. et al. Pharmacy career deciding: making choice a 'good fit'. *Journal of Health Organisation and Management* (2009) **23** 85–102.
177. Hassell, K. et al. Measuring job satisfaction of UK pharmacists: a pilot study. *International Journal Pharmacy Practice* (2007) **15** 259–264.
178. Hassell, K. et al. Part of a global workforce: migration of British-trained pharmacists. *Journal of Health Services Research and Policy* (2008) **13** (Suppl 2) 32–39.
179. Hassell, K. and Shann, P. The national workforce census: (3). The part-time pharmacy workforce in Britain. *Pharmaceutical Journal* (2003) **271** 58–59.
180. Shann, P. and Hassell, K. Flexible working: understanding the locum pharmacist in Great Britain. *Research in Social and Administrative Pharmacy* (2006) **2** 388–407.
181. Hassell, K. et al. The complexities of skill mix in community pharmacy. *Pharmaceutical Journal* (2002) **269** 851–854.
182. Eden, M. et al. Workload pressure among recently qualified pharmacists: an exploratory study of intentions to leave the profession. *International Journal of Pharmacy Practice* (2009) **17** 181–187.
183. Schafheutle, E.I. et al. Factors influencing pharmacist performance: a review of the peer-reviewed literature. *Health Policy* (2011) **102** 178–192.
184. Schafheutle, E.I. et al. Learning professionalism through practice exposure and role models. *Pharmaceutical Journal* (2011) **285** 164–166.
185. MacDonald, R. et al. *The impact of incentives on the behaviour and performance of primary care professionals. A report for the National Institute for Health Research Service Delivery and Organisation programme*. Queen's Printer and Controller of HMSO, London (2010).
186. Hassell, K. et al. Workload in community pharmacies in the UK and its impact on patient safety and pharmacists' well-being: A review of the evidence. *Health and Social Care in the Community* (2011) **19** 561–575.
187. Willis, S. et al. What is the evidence that workload is affecting hospital pharmacists' performance and patient safety? Centre for Workforce Intelligence, London (2011).
188. Seston, E. and Hassell, K. Workforce update – joiners, leavers, and practising and non-practising pharmacists on the 2010 Register. *Pharmaceutical Journal* (2011) **286** 473–476.
189. Gidman, W. et al. The impact of increasing workloads and role expansion on female community pharmacists in the UK. *Research in Social and Administrative Pharmacy* (2007) **3** 285–302.
190. Willis, S. et al. Identifying the risks and opportunities associated with skill mix changes and labour market substitution in pharmacy. Centre for Workforce Intelligence, London (2011).

191. Holland, R. et al. Effectiveness of visits from community pharmacists for patients with heart failure: HeartMed randomised control trial. *British Journal of Clinical Pharmacology* (2007) **65** 303–316.
192. Koshman, S.L. et al. Pharmacist care of patients with heart failure: A systematic review of randomised trials. *Archives of Internal Medicine* (2008) **168** 687–694.

7. GLOSSARY

- API** – active pharmaceutical ingredient is any substance that is represented for use in a drug and that, when used in the manufacturing, processing or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug. APIs include substances manufactured by processes such as (1) chemical synthesis; (2) fermentation; (3) recombinant DNA or other biotechnology methods; (4) isolation/ recovery from natural sources; or (5) any combination of these processes.
- Adaptive clinical trials** – clinical trials in which the design or analysis of the clinical trial may change during the trial as a consequence of interim results.
- Adherence** – the extent to which a patient’s behaviour matches the agreed recommendations from the prescriber. Intentional non-adherence occurs when the patient decides not to take the medication or to take it in a way that differs from the recommendations. Unintentional non-adherence occurs when a patient is prevented from implementing their intention to take the medication, as prescribed, by factors beyond their control or when they forget.
- Adjuvant** – substance that enhances the activity of another. It is frequently used to describe the actions of chemicals, such as aluminium salts, to enhance the activity of vaccines.
- Adverse drug event** – refers to any injury caused by a drug and any harm associated with the use of a drug. Adverse drug events can be preventable (for example, a wrong dose leading to injury) or non-preventable (for example, an allergic reaction occurs in a patient not known to be allergic). Non-preventable adverse drug events are also often termed adverse drug reactions.
- AWMSG** – All Wales Medicines Strategy Group. Provides advice on medicines management and prescribing to the Minister for Health and Social Services. It develops independent and authoritative advice on new medicines and advises the Welsh Assembly on future developments in healthcare and on the development and implementation of a prescribing strategy for Wales.
- Antibiotic** – an antibiotic is a compound produced by an organism (often a bacterium or mould). Antibiotic classes include penicillins, cephalosporins, tetracyclines, aminoglycosides and macrolides which are used to treat bacterial infections. Semi-synthetic antibiotics were developed through minor chemical modifications of the original antibiotic. The term antibiotic, however, is now commonly used to describe any agent used to treat bacterial infections irrespective of whether they were initially isolated from a natural source or created using a completely synthetic process.
- Antimicrobial** – an agent that can kill or inhibit the growth of microorganisms such as bacteria, fungi, viruses and protozoa. Antimicrobial agents can be obtained from a natural source or produced synthetically.
- Antimicrobial stewardship** – includes both the management of antimicrobials and infection control measures. The aim of antimicrobial stewardship is to make the best use of antimicrobials to manage infection, so as to ensure optimal outcomes and minimal harm to patients and the wider society.
- Antivirulence drugs** – drugs which prevent disease by neutralising virulence factors, the specific proteins or toxins that a pathogen uses to establish an infection.
- Bacteriophage** – a virus that infects bacteria and replicates within the host, and usually destroys the bacteria by lysis releasing new viruses. Many varieties of bacteriophage exist and usually each one only attacks one kind of bacteria.
- Bioavailability** – the rate and extent to which an administered dose of drug or other substance reaches the general circulation. It is usually expressed as the fraction of the administered drug that is available to produce a pharmacological effect.
- Bioequivalent** – a medicine that does present a known or potential bioequivalence problem and meets an acceptable *in vitro* standard, or, if the medicine does present a known or potential problem, it has been shown to meet an appropriate bioequivalence standard.

- Bioequivalence** – two medicines whose rate and extent of absorption differ by $\pm 20\%$ or less OR the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molecular dose under similar conditions in an appropriately designed study.
- Biologic (or Biological product)** – a polypeptide, protein or nucleic acid-based pharmaceutical substance. Biologics are larger and have more complex structures than the more common low molecular weight drugs and include a wide range of products including vaccines, blood and blood components, allergens, somatic cells, genes, gene therapy medicines, tissues and proteins.
- Biomarker** – a substance that is an indicator of a biological process. Laboratory measurement of the biomarker can be used to assess the presence or progress of disease or the response to a therapeutic intervention.
- Biomacromolecule** – an organic molecule produced by living cells, e.g. a protein, carbohydrate, lipid or nucleic acid.
- Biopharmaceutics** – study of the physical and chemical properties of drugs and their dosage forms as related to the onset, duration and intensity of drug action.
- Biosimilar (or Biosimilar agent)** – a product 'highly similar' to an already-approved biological product. A version of an innovator biological product marketed following expiry of the original patent. Due to the molecular complexity of biological products, biosimilars are unlikely to ever be identical to the innovator product.
- Blockbuster** – an extremely successful medicine that generates annual sales of at least \$1 billion for the company that created it.
- Carbon nanotubes** – extremely thin hollow cylinders made of carbon atoms, which have a diameter in the nanometre range but may be up to micrometres long. Carbon nanotubes are extremely strong and stiff and are being investigated for drug delivery, gene delivery and biosensor applications.
- Children** – a heterogeneous population group ranging from neonates to adolescents (16 to 18 years of age).
- Chiral** – a structural characteristic of a molecule. A molecule is chiral if it is impossible to superimpose it on its mirror image.
- Clinical pharmacokinetics** – the application of pharmacokinetic principles to the safe and effective therapeutic management of medicines in an individual patient.
- Clinical research** – research on the safety and effectiveness of medicines in practice.
- Cochrane review** – a systematic review presenting up-to date summaries of research in healthcare and health policy and published in *Cochrane Database of Systematic Reviews*. Cochrane reviews determine the healthcare benefits and risks of a particular procedure, intervention or medicine and the accuracy of diagnostic tests, as well as assessing methodologies used in systematic reviews and clinical trials.
- Cold chain** – refers to the management of temperature-sensitive products that must be kept within a defined temperature range as they move through the supply chain, i.e. during distribution and storage. It applies to medicines, particularly vaccines, for which irreversible damage can occur if stored outside of a specified temperature range, usually refrigerated conditions.
- Companion diagnostic** – a diagnostic test that is developed specifically to assist with decision-making in relation to the prescribing of a particular drug. An example would be the test for over-expression of the human epidermal growth factor 2 (HER-2) in a tumour prior to prescribing the anti-cancer drug, trastuzumab.
- Concordance** – partnership in medicines taking, and relates to shared decision-making about medicines between a patient and a healthcare professional.
- Counterfeit medicine** – is a medicine that does not comply with intellectual property rights or that infringes trademark law.
- De novo** – a Latin expression meaning 'from the beginning'. It is used in medicinal chemistry to describe the synthesis of complex molecules from simple starting materials.
- Dissolution** – process by which a drug, usually in the solid state, dissolves in solution in its molecular form.

- DNA microarray analysis** – technique that allows the expression levels of hundreds or thousands of genes within a cell to be determined in a single experiment.
- Drug discovery and design** – process by which potential drugs are discovered or designed. Many drugs have been discovered either by isolating the active ingredient from natural products or by serendipity. Modern drug discovery focuses on understanding the metabolic pathways related to a disease or a pathogen and using molecular biology or biochemistry to manipulate these pathways.
- Drug development** – activities undertaken after a molecule is identified as a potential drug in order to establish its suitability as a medicine. Drug development includes determining physicochemical properties and appropriate formulation, efficacy and safety, and clinical trial work. A combination of *in vitro* studies, *in vivo* studies and clinical trials are performed as part of the development process.
- Drug (molecule)** – traditionally refers to small, organic molecules and peptides that exert a pharmacological effect and are typically made through standard chemical methodology. The term has now been expanded to include biologics.
- Drug repurposing** – development of novel uses for existing small molecule drugs. This process has the benefit of reducing the risks of failure associated with drug development as the drug has already passed a significant number of tests (including toxicity).
- Drug rescue** – refers to research involving small molecules and biologics whose development was abandoned before they were marketed as medicines, with the aim of identifying new therapeutic uses. Compounds that enter the drug rescue process may, but not necessarily, have detailed information about their pharmacology, formulation, dosing and potential toxicity.
- EMA** – European Medicines Agency. A decentralised agency of the European Union responsible for the scientific evaluation of applications for European Union marketing authorisations for human and veterinary medicines.
- Endogenous** – originating or produced within an organism, tissue or cell.
- Epigenetics** – changes in gene expression that are stable between cell divisions, and sometimes between generations, but do not involve changes in the underlying DNA sequence of the organism. It is a term used to describe the idea that environmental factors can cause an organism's genes to behave (or 'express themselves') differently, even though the genes themselves do not change.
- Excipient** – an ingredient in a pharmaceutical formulation other than the active ingredient. An excipient is used in a formulation to confer specific properties, e.g. to act as a lubricant, disintegrant or stabilising agent.
- Expert patients** – people living with a long-term health condition who are able to take more control over their health by understanding and managing their conditions, leading to an improved quality of life. Expert patients manage their conditions in partnership with healthcare professionals, communicate effectively, are willing to share responsibility for treatment and are realistic about the impact of the disease on themselves and their families.
- Falsified medicines** – fake medicines that pass themselves off as real, authorised medicines. A falsified medicine may contain ingredients of low quality or in the wrong doses; be deliberately and fraudulently mislabelled with respect to their identity or source; have fake packaging, the wrong ingredients or low levels of the active ingredients. A falsified medicine would not pass the usual regulatory evaluation of quality, safety and efficacy.
- FDA** – The United States Food and Drug Administration. The FDA assures the safety and effectiveness of human and veterinary medicines, vaccines and other biological products, medical devices, food supply, cosmetics, dietary supplements, and products that give off radiation. The FDA regulates medicines licensed for use in the United States.
- Flow chemistry** – process of performing chemical reactions in a continuously flowing stream rather than as a batch.
- Generic drug** – internationally approved name of an active pharmaceutical ingredient, which is no longer protected by a patent and is available in one or more generic medicines or dosage forms.

- Generic medicine** – applies only to medicines containing small-molecule drugs that are the same as, and bioequivalent to, an already approved innovator product containing a small-molecule drug. Generic medicines can only be marketed once the innovator product is off patent.
- Genotoxic** – chemicals or other agents that damage cellular DNA, resulting in mutations which can lead to cancer.
- Healthcare professional** – any regulated professional including specialists, general practitioners, pharmacists, nurses and other allied health professionals delivering healthcare to patients.
- Health literacy** – degree to which an individual has the capacity to obtain, process, understand and use healthcare information to make appropriate healthcare decisions and follow instructions for treatment.
- Health services research** – research that identifies the most effective way to ensure safe, high quality patient care.
- Immunogenicity** – ability of an antigen to induce an immune response.
- Innovation platform** – bringing together of stakeholders focused on a particular challenge or activity with the aim of integrating available technologies and better coordinating of policy and procurement to enable a significant change in the quality of services and the ability of businesses to provide solutions for the global market. Innovation platforms are a new way of working for Government and business and are an opportunity to bring business and Government closer together to generate innovative solutions to policy and societal challenges.
- Innovator product** – original branded medicine that contains a new drug substance. It is a medicinal product that is authorised and marketed on the basis of submission of a full dossier of information, including chemical, biological, pharmaceutical, pharmacological, toxicological and clinical data.
- In silico** – a Latin expression for methods of evaluating drugs and medical interventions using computer models rather than laboratory experiments. Computation models have been used in the discovery of novel drug molecules, in pharmacokinetics, in assessing toxicity and in physicochemical characterisation.
- Isomers** – two or more molecules that are composed of the same elements in the same proportions (i.e. the same chemical formula) but which have different arrangements of the elements in the molecule resulting in different properties.
- Liposome** – small, hollow, water-filled spherical structures dispersed in water and whose walls consist of bilayers of phospholipids. Liposomes may be unilamellar (containing a single bilayer) or multilamellar (composed of many bilayers) and are used as vehicles to deliver a range of agent including small molecule drugs, peptides, proteins and nucleic acids.
- Marketing authorisation** – medicines which meet the standards of safety, quality and efficacy defined by the appropriate regulatory agency are granted a marketing authorisation (previously a product licence), which is necessary before the medicines can be prescribed or sold and covers all the main activities associated with the marketing of a medicinal product. In the UK, the relevant body is the Medicines and Healthcare Products Regulatory Agency.
- Medicine or medicinal product** – any substance or combination of substances having properties for treating or preventing disease in human beings or any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis. In the context of the present report, a medicine is the drug-containing product given to the patient, i.e. the formulated product.
- Medical device** – covers a wide range of devices from highly sophisticated computerised medical equipment down to simple wooden tongue depressors; some eye drops, topical ointments and contact lens products are classed as medical devices.
- MHRA** –the Medicines and Healthcare Products Regulatory Agency. Responsible for regulating all medicines and medical devices in the UK by ensuring they work and are acceptably safe. The work of the MHRA is underpinned by science and research, which enables robust and fact-based judgements to be made that ensure the benefits justify any risks to patients and the public.

Medicines management – includes the clinical, cost-effective and safe use of medicines to ensure that patients get the maximum benefit from the medicines they need, while at the same time minimising potential harm.

Medicines optimisation – an approach that improves patient outcomes through maximising the use of medicines in preventing disease or the progression of disease and which aims to ensure patients get the greatest health gain and least harm from their medicines.

Medicines reconciliation – process of obtaining an up-to-date and accurate list of a patient's medicines that has been compared to the most recently available information and has documented any discrepancies, changes, deletions and additions.

Medicines review – process by which a healthcare professional and a patient discuss the patient's medicines and medicine-taking behaviour; it is usually performed face to face but can be performed remotely if necessary. Medicines review can be used to identify medicines that are no longer required and medicines that should be used.

Micelle – a self-assembling complex of surfactants: molecules that possess both polar and non-polar portions. Micelles have a size in the nanometre range and are often used to solubilise poorly water-soluble compounds.

Microreactor – small device in which chemical reactions take place. Microreactors are based on continuous flow chemistry, with reactors often having a height and width of less than 1mm and a length of between 1cm and 1m. Chemical reactions occur continuously, enabling high product of yields per hour – making them suitable for large scale production. The technology has been used to prepare drug substances.

Modernising Pharmacy Careers – programme launched in England in February 2009, designed to ensure the pharmacy workforce has the knowledge, skills and capacity to deliver the services necessary in the future for patients and the public. A core part of Modernising Pharmacy Careers is the development and implementation of a new approach to pharmacist undergraduate education and pre-registration training.

Monogenic disease – a hereditary disease caused by a genetic trait that is controlled by a single gene.

Nanomedicine – application of nanotechnology in making a medical diagnosis or treating or preventing disease. It exploits the improved and often novel physical, chemical and biological properties of materials at the nanometre scale.

Nanoparticle – a discrete nano-object where *all* three Cartesian dimensions are less than 100 nm. Nanoparticles are made from a variety of materials that have been investigated for a variety of medicines and diagnostic applications. Compared to the properties of the bulk material, nanoparticles have novel properties, primarily as a result of their increased surface area.

Near patient testing – a test designed to be used at, or near to, where the patient is. Tests may range from simple dipstick tests to sophisticated analysers. Significantly, non-laboratory-based healthcare professionals perform the tests and the results are generated quickly.

NICE – National Institute for Health and Care Excellence (NICE) produces evidence-based guidance that evaluates the clinical efficacy and cost-effectiveness of medicines, treatments, procedures and devices and determines those that offer the best value for money for the NHS. NICE also produces public health guidance recommending best ways to encourage healthy living, promote well-being and prevent disease.

NMR spectroscopy – technique that gives detailed information about the molecular motion and interaction profile of a molecule based on the interactions of nuclear magnetic moments with electromagnetic radiation. It is an important technique in drug development and is mainly used to investigate the properties of organic molecules and biological molecules.

Number needed to treat (NNT) – number of patients that need to be treated to prevent one additional bad outcome, e.g. death, stroke. If a drug has a Number Needed to Treat of 5, it means you have to treat five patients with the drug to prevent one additional bad outcome.

- Number needed to harm (NNH)** – number of patients that would need to be treated over a specific period of time before one bad outcome of the treatment will occur. If a drug has a Number Needed to Harm of 100, it means that for every 100 patients treated there will be one additional bad outcome.
- ‘Off-label’** – medicines with a UK marketing authorisation (previously a product licence), which are prescribed for an unlicensed indication, i.e. are used outside the terms of the marketing authorisation for the medicine. Examples of ‘off-label’ use include a different route of administration, a different dosage (either higher or lower), a different indication, or use in a patient group not covered by the marketing authorisation.
- Parenteral administration** – administration of a drug or medicine by a route other than through the gastro-intestinal tract. Parenteral administration includes injections, ophthalmic delivery, pulmonary delivery and transdermal delivery. The term parenterals is often incorrectly used to describe only injectable preparations.
- Patent box** – UK Government initiative where the effective rate of corporation tax is reduced to 10% for income from patents. Its aim is to encourage innovation by providing an incentive for companies to locate jobs associated with the development, manufacture and exploitation of patents in the UK.
- Personalised/Stratified medicine** – exploitation of the knowledge of a patient’s genetic make-up to determine whether or not a drug will be effective in treating that patient, or alternately produce unwanted, adverse effects.
- Pharmaceutical science** – is the science of medicines development and use and applies basic, applied and social sciences to the discovery, design, formulation and optimal use of medicines in patients. Pharmaceutical science involves components of many sciences, including the chemical, physical and biological sciences, mathematics and statistics, and engineering.
- Pharmacodynamics** – the effect of drugs in the body. The study of the biochemical and physiological effects of drugs and the mechanism(s) of their actions, including the correlation of their actions and effects with their chemical structure.
- Pharmacoepidemiology** – the use and effects of the medicines in large patient populations.
- Pharmacokinetics** – how the body handles a drug, i.e. its absorption, distribution, metabolism and excretion.
- Pharmacogenetics** – study or clinical testing of genetic variation that gives rise to differing response to drugs.
- Pharmacogenomics** – application of genomic technologies to new drug discovery and further characterisation of older drugs.
- Pharmacoeconomics** – evaluating the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or enhanced quality of life) of a pharmaceutical product.
- Pharmacovigilance** – continual monitoring of medicines during their lifetime as therapeutic agents.
- Pharmaceutical care** – the responsible provision of drug therapy to achieve agreed outcomes that improve an individual’s quality of life. It involves cooperation with the patient and, if appropriate, their carer and other professionals in designing, implementing and monitoring a pharmaceutical care plan that will produce a specific therapeutic outcome for the patient.
- Pharmaceutical equivalence** – medicines that contain identical amounts of the same active drug ingredient in the same dosage form and route of administration, and meet standards of strength, quality, purity and identity.
- Pharmaceutical practice** – the contribution made by pharmaceutical scientists and pharmacists to health improvement through the creation of new and improved medicines and in helping patients to make the best use of their medicines.
- Pharmaceutical public health** – application of pharmaceutical knowledge, skills and resources to the science of preventing disease, prolonging life, and promoting and improving health for all through organised activities of society.
- Pharmacy robots** – machines that enable some pharmacy processes to be automated. They are useful in medication ordering, they streamline the dispensing and medicines supply processes and reduce stock holding.

Polydispersity – measure of the heterogeneity of sizes of molecules or particles in a mixture. A sample that has an inconsistent size, shape and mass distribution is defined as polydisperse.

Polygenic disease – illness caused by multiple genes.

Polypharmacy – use of multiple medicines in a patient who has a number of concomitant medical conditions. The use of polypharmacy is particularly common in older patients.

Primary care – this is a multidisciplinary aspect of healthcare with a whole range of professionals, such as the local healthcare people receive from GPs, pharmacists, dentists, optometrists and nurses. These are the services that most often bring people into contact with the NHS.

Process analytical technology – system for designing, analysing and controlling manufacturing processes based on an understanding of the scientific and engineering principles involved and identification of the variables which affect product quality.

Proteomics – application of molecular biology, biochemistry and genetics to the analysis of the structure, function and interactions of the proteins produced by the genes of a particular cell, tissue or organism.

Quality by design – systematic approach to pharmaceutical development that begins with predefined objectives for the product, following which formulations and manufacturing processes are designed and developed to ensure the predefined product specifications are met. The process of quality by design is scientifically-based and uses quality risk management.

Quantum dots – nanostructures, often made from metals or nanocrystals, that have unique optical and electronic properties. Quantum dots have been proposed for the controlled release of drugs, as well as diagnostic and biosensor applications.

Regenerative medicine – process of replacing or regenerating human cells, tissues or organs to restore or establish normal function through supporting and activating the body's natural healing. The field brings together a variety of disciplines, including cell therapy, tissue engineering, biomaterials engineering, growth factors and transplantation science.

Risk sharing schemes – also known as patient access schemes. Involves an agreement between those purchasing medicines and the pharmaceutical companies to ensure health gains are maximised within finite budgets. Sometimes payment is made to the pharmaceutical company only if the medicine delivers the anticipated health outcome in a patient.

Secondary care – this is the healthcare that people receive in hospital and may be unplanned emergency care or surgery, or planned specialist medical care or surgery. If people go to hospital for planned medical care or surgery, this will usually be because their GP, or another primary care health professional, has referred them to a specialist.

SMC – Scottish Medicines Consortium. Provides advice to NHS Boards and their Area Drug and Therapeutics Committees across Scotland on the clinical and cost-effectiveness of newly licensed medicines, new formulations of existing medicines and new indications for established products.

'Specials' manufacturer – manufacturer of 'special' medicines. A company must hold a specials manufacturer's licence, which is granted by the MHRA.

'Special' medicines – unlicensed medicines prepared to meet the need of an individual patient, where a suitable licensed medicine is not available. 'Specials' are usually manufactured by a 'specials' manufacturer holding a specials manufacturer's licence, either in multiple quantities with end product testing or as a bespoke medicine without end product testing. Alternatively, 'specials' can be extemporaneously prepared in a pharmacy under the direct supervision of a pharmacist.

Stratified medicine – exploitation of the knowledge of a patient's genetic make-up to determine whether or not a drug will be effective in treating that patient, or alternately produce unwanted, adverse effects.

Systems biology – study of the behaviour of complex biological organisation and processes in terms of molecular constituents. It involves focusing on the complex interactions between key elements such as DNA, RNA, proteins and cells with respect to one another.

Systems pharmacology – how drugs work (on specific pathways, on different cell types and in different organs/diseases), what the variability in patient response is and why treatments fail.

Theranostic – diagnostic test directly linked to the application of a specific therapy. It provides critical information that determines whether a new medicine is appropriate for a patient, or enables a current treatment to be individually tailored.

Therapeutic equivalence – when classified as therapeutically equivalent, medicines will be approved as safe and effective, as well as being pharmaceutical equivalents and bioequivalent.

Therapeutic vaccine – vaccine against a chronic infectious disease such as HIV-related diseases and tuberculosis, as well as gastric ulcers, cancer and autoimmune diseases. In a therapeutic vaccine, a molecule closely related chemically to the etiological agent that causes the disease stimulates an immune response directed against the causative agent. This situation is analogous in a conventional vaccine. To date, therapeutic vaccines are available for treatment of prostate cancer and multiple sclerosis.

Therapeutic index – ratio of the amount of a drug that causes the therapeutic effect to the amount that causes death (in animals) or toxicity (in humans). Therapeutic index is used as a measure of the relative safety of the drug for a particular treatment.

Vesicular formulations – mixture of molecules, including phospholipids or surfactants, which when mixed together, and processed under suitable conditions, form hollow, water-filled spherical structures possessing a bilayer.

8. APPENDIX

8.1 List of Challenges

Below is a list of all the Challenges and which page they are included on within this report.

CHALLENGE	CHALLENGE STATEMENT	PAGE
1	Ensure excellence in the development of medicines by fostering and promoting world-leading pharmaceutical science	17
2	Reduce the time and cost to market of a medicine	17
3	Understand the target population better to develop better, safer and more effective medicines	17
4	Ensure patient safety: from drug discovery to medicines administration to patients	19
5	Secure and strengthen the UK's position as a major player in the global pharmaceutical industry	20
6	Build upon academic-hospital-industrial and industrial-industrial partnerships to develop new and innovative approaches for drug discovery	20
7	Encourage new Government initiatives to support the UK science base	20
8	Improve the drug discovery process by effectively harnessing new information and technologies	23
9	Improve methods to correlate target validation with desired clinical outcomes	23
10	Identify the genetic defects associated with specific diseases and the role of genetics, the environment and lifestyle on disease development	23
11	Produce reliable and predictive physiologically-based pharmacokinetic modelling techniques to optimise the hit-to-lead process	24
12	Increase the likelihood of developing a medicine by optimising its absorption, distribution, metabolism, excretion and toxicity	24
13	Develop new antimicrobials and new approaches to treating antimicrobial infections	28
14	Encourage initiatives to develop new medicines for the treatment of neglected diseases, including identifying new funding streams to promote not-for-profit medicines research in neglected diseases	28
15	Encourage initiatives that support the repositioning and repurposing of drugs, where possible, for patient benefit	30

CHALLENGE	CHALLENGE STATEMENT	PAGE
16	Improve the formulation and delivery of drugs and the development of more reliable predictive and modelling methods to optimise formulations	30
17	Improve the formulation and delivery of small molecule drugs through developing and implementing simple and commercially viable technologies	33
18	Optimise the formulation, delivery and manufacture of biologics to make products affordable	34
19	Improve the stability of and optimise the immune response to vaccines	34
20	Exploit the properties of nanomaterials to develop safe, advanced medicines	34
21	Work to improve the range of excipients available for use in pharmaceutical formulations	36
22	Develop and implement new and innovative technologies for the delivery of small molecule drugs and biologics, which may incorporate feedback-control	36
23	Educate the public and patients about the ethical and moral issues surrounding the use of new technologies	39
24	Expand the concept of personalising medicines for all patients	39
25	Improve targeting of medicines to specific populations through the use of biomarkers with the aim of reducing attrition rates during medicines development	39
26	Develop models that encourage innovation in stratified medicines, which embrace economic, regulatory and ethical issues and make cost-effective treatment available to patients	39
27	Promote clinical trials in specific populations to ensure the dose is right for the patient	40
28	Develop age-appropriate dosages and formulations based on pharmacokinetic, pharmacodynamic and pharmacogenomic information	42
29	Develop patient-centred medicine including combination formulations	42
30	Increase the research capacity and capability within the profession	43
31	Develop effective methods for assessing patients' medicines needs to improve the safe, effective and efficient use of medicine thereby optimising their use	48
32	Increase the involvement of pharmacy in prescribing and review of medicines use, including more roles for the pharmacist as an independent prescriber	48
33	Establish an evidence-based approach to all OTC advice and medicines supply	48
34	Improve communication skills of pharmacists and their staff	48
35	Introduce a culture of intervention recording and involvement in post-authorisation studies of OTC medicines	48
36	Develop strategies and research evidence to improve patient adherence to medicines	51

CHALLENGE	CHALLENGE STATEMENT	PAGE
37	Facilitate partnerships between the patient, their carers (where appropriate) and the multidisciplinary team in medicines taking	51
38	Provide patients with accessible and readable information, which describes the chance of benefit and the risk of harm, allowing them to make informed decisions about whether a medicine is right for them	52
39	Support patients to become well informed about their medicine taking and respect the needs of the expert patient	52
40	Improve understanding of the medication and pharmaceutical care needs of children	54
41	Increase understanding of the causes of medication errors and the impact of pharmacy interventions	55
42	Manage medicines appropriately to achieve optimal outcomes in vulnerable patient groups, such as young and older patients	57
43	Increase pharmacy's evidence-based contribution to health improvement, in particular in the community pharmacy setting	58
44	Reduce smoking, obesity and alcohol consumption – a challenge for all health professionals	58
45	Ensure that currently available antibiotics are used appropriately, and encourage the understanding of good hygienic practices	60
46	Maintain the maximum effectiveness of currently available antimicrobials through antimicrobial stewardship	60
47	Build on the available evidence base to further elucidate the role of pharmacy in supporting drug misusers	60
48	Further integrate pharmacy immunisation services into the NHS	61
49	Expand the pharmacy vaccination services to include patients in the 'at risk' categories who prefer this venue	61
50	Find new complementary ways to facilitate earlier identification of adverse events	62
51	Increase pharmacy's evidence-based contribution to earlier diagnosis of chronic disease and greater involvement in patient screening	62
52	Contribute to the evidence base evaluating the relative risks and benefits of screening for diseases	62
53	Provide equitable access to medicines and pharmacy services to all patients globally	63
54	Minimise the barriers to the responsible global re-use of medicines	63
55	Reduce the development and spread of disease in the developing world	64

CHALLENGE	CHALLENGE STATEMENT	PAGE
56	Improve access to quality assured medicines in the developing world, including reducing counterfeiting	65
57	Ensure the UK remains an attractive location for the pharmaceutical industry to undertake medicines research and development	68
58	Encourage greater collaboration amongst large pharmaceutical companies, SMEs and universities to support drug discovery and medicines innovation	68
59	Support the UK pharmaceutical industry to remain a major and competitive player in global research and development	69
60	Encourage medicines regulators in the UK and EU to promote Quality by Design (QbD)-enabled development programmes and filings	69
61	Develop medicines licensing processes that enable timely changes to materials, manufacturing processes and analytical test methods arising from continuous improvement initiatives	69
62	Maintain the integrity of the medicines supply chain in the UK through joint working of all stakeholders	69
63	Develop novel regulatory systems that expedite the marketing authorisation process for innovative therapies	70
64	Develop new NHS models of medicines reimbursement that give patients timely access to new medicines, while enabling the pharmaceutical industry to invest in future medicines innovation	70
65	Increase the number of patients participating in clinical trials in the UK	71
66	Develop processes that ensure transparency in clinical trials and that the publication of all clinical trial data is available in the public domain in a suitable format	72
67	Support well-conducted pharmacy-based intervention studies conducted in line with the MRC Framework	73
68	Strive for adequate funding to support research in all aspects of the pharmaceutical sciences	73
69	Identify the causes of and solutions to workplace pressures	75
70	Identify future demand for pharmaceutical services and expertise globally, including qualified persons (QPs), clinical pharmacologists, academics, locum pharmacists and pharmaceutical scientists	77
71	Measure the effectiveness of the entire pharmacy workforce	78

8.2 List of Vignettes

Below is a list of the vignettes and which page they are included within this report.

TITLE	VIGNETTE	PAGE
THE ROLE OF PHARMACEUTICAL SCIENTISTS	Medicines have revolutionised the treatment of disease, reduced the need for hospitalisation and surgery, and improved the quality of life of patients. Pharmaceutical scientists have been instrumental in the discovery of new drugs and the development of novel medicines for the treatment of many conditions, including asthma, peptic ulcers, migraines and cancer and in developing new and improved vaccinations.	12
DRUG TESTING IN SPORT	One of the world's leading drug control laboratories is the Drug Control Centre at King's College London. The current Director is pharmacist Prof. David Cowan, who, together with Prof. Arnold Beckett, founded and co-directed the laboratory when it opened in 1978, funded by the Sports Council. An important part of the Centre's function is to develop new methods for detecting doping in sport and then apply them to analyse samples from sports competitions. In the lead up to the 2012 London Olympic and Paralympic Games, GlaxoSmithKline funded the Drug Control Centre to help develop new screening techniques that would be world leading in the field of drug testing. The techniques that resulted were announced as super-fast and super-sensitive and allowed the Centre to test over 6000 samples during the Games. Such was the deterrent value of the tests the Drug Control Centre developed that the 2012 London Olympic and Paralympic Games were the cleanest Games ever in terms of drug use. As Prof. Cowan said at the time, "If you cheat – we will catch you." Prof. Cowan was awarded the Pharmaceutical Scientist of the Year Prize by the Royal Pharmaceutical Society in 2013.	15
MEDICATION ERRORS	Medication errors are one of the leading causes of injury to patients, leading to increased morbidity and mortality as well as an economic burden to health services. The 'gold standard' for assessing the clinical significance of medication errors was developed by pharmacist Professor Briony Dean Franklin. For nearly 20 years, Prof. Franklin has been involved with medication safety research and has published widely in this field Prof. Franklin is currently Professor of Medication Safety at the UCL School of Pharmacy and Director of the Centre for Medication Safety and Service Quality (CMSSQ), a joint NHS and academic research unit. These roles allow her to combine her interests in research, education and training, and hospital clinical pharmacy practice. In recognition of her research into medicine safety, Prof. Franklin was awarded the Royal Pharmaceutical Society's Practice Research Medal in 2005.	18

TITLE	VIGNETTE	PAGE
ADVANCING DRUG DISCOVERY	<p>The discovery of sumatriptan, the first in a new class of drugs for the treatment of migraine, has been described as the most important achievement in the treatment of headache in the last 50 years. It was Dr Pat Humphrey's work on cerebrovascular pharmacology that led to the development of sumatriptan. Dr Humphrey, a pharmacy graduate, had joined Allen and Hanbury's in 1972, becoming Director of Pharmacology at Glaxo in 1983. Dr Humphrey was also instrumental in the discovery of several other drugs, including naratriptan (migraine), alosetron (symptoms of irritable bowel syndrome), ondansetron (nausea and vomiting) and salmeterol (asthma). More recently, as Founder and Head of Research at Theravance (US), and through his involvement with Verona Pharma PLC, Dr Humphrey has continued his involvement in the discovery of new drugs. In recognition of his work, Dr Humphrey has received many awards, including the Royal Society's Mullard Medal in 1997 and an OBE for his services to migraine research.</p>	20
DEVELOPMENT OF A NEUROMUSCULAR BLOCKING AGENT FOR USE IN ANAESTHESIA	<p>In surgical procedures it is often necessary to relax the body muscles, particularly in the abdomen. Although this can be achieved with some of the dart and arrow poisons used by aboriginal hunters, these poisons result in a long-lasting muscle paralysis, including the diaphragm, so that the patient cannot breathe unaided. Prof. John Stenlake, a graduate of the London School of Pharmacy working at Strathclyde University, secured a Medical Research Council grant to investigate potentially shorter-acting muscle relaxants by a mechanism known as Hofmann elimination. Pharmacist Dr Roger Waigh was initially employed on the grant, but quickly showed that the original rationale would not work. He found an alternative which led to synthesis of a series of highly active relaxants, prepared under his supervision first by Dr John Urwin, a pharmacist from Nottingham University, and then by George Dewar, another pharmacist from Strathclyde University who prepared atracurium as part of his PhD studies. For several years, atracurium was the market leader worldwide and is still used for long operations, particularly in the elderly. Professor Stenlake was awarded the Mullard medal of the Royal Society.</p>	21

TITLE	VIGNETTE	PAGE
REVOLUTIONARY NEW DRUG THERAPIES	<p>Glaxo was transformed from unglamorous beginnings as a producer of powdered milk for infants into one of the world's largest and most profitable manufacturers of prescription medicines by pharmacist Sir David Jack and his team. Sir David joined Allen and Hanbury's as head of research in 1961. He considered that Glaxo's traditional strategy of licensing drugs from foreign companies was unsustainable in an increasingly global industry and that the treatment of common disorders, that robbed patients of a good quality of life, had to be tackled as a matter of priority. His team therefore concentrated on treatments for respiratory, cardiovascular and gastrointestinal tract diseases. Sir David's first success was the discovery of the bronchodilator salbutamol in 1966, a new effective asthma rescue therapy launched as Ventolin in 1969. A decade later, in May 1976, his team produced ranitidine hydrochloride, a treatment for gastric and duodenal ulcers. A supremely efficient development programme followed, lasting just five years, and Zantac was launched in 1981 to become the first 'blockbuster' drug, generating sales of over \$1 billion annually. Sir David was recognised with a CBE in 1982, the Royal Society's Mullard Medal in 1991, an FRS in 1992 and a knighthood in 1994 for his services to patients and commercial success of his scientific and strategic brilliance.</p>	22
DEVELOPMENT OF NEW ANTI-CANCER MEDICINES	<p>The discovery and development of new anti-cancer drugs with novel chemical structures and/or modes of action is essential for improving the treatment of cancer. Professor Malcolm Stevens has successfully used his pharmaceutical science knowledge to create new anti-cancer drugs that possess three qualities, namely a novel mechanism of action, an ease of synthesis and a pharmaceutical robustness. Using this approach, Prof. Stevens has been responsible for taking several new experimental cancer drugs into the clinic, two of which reached the market, namely: bropirimine (Remisar), an immunomodulatory and antiviral agent which triggers cytokine cascades and temozolomide (Temodal) which is primarily used to treat glioblastoma, the most common adult brain tumour. Total worldwide sales of Temodal (without generic versions) have exceeded \$8.5 billion. In line with Prof. Stevens' philosophy in creating new anti-cancer drugs, temozolomide possesses three qualities: an ability to change gene expression through selective methylation of DNA, synthesis using a two-stage process and oral administration at out-patient clinics. Indeed, the commercial synthesis is the original synthesis developed in 1980 by PhD pharmacist Robert Stone. In recognition of his outstanding contribution to cancer research, Prof. Stevens has received many awards, including the 1994 Royal Pharmaceutical Society's Harrison Memorial Medal, an OBE in 1999 for his achievements in anti-cancer drug design and an FRS in 2009.</p>	23

TITLE	VIGNETTE	PAGE
CONTINUOUS MANUFACTURING	<p>The Centre for Continuous Manufacturing and Crystallisation (CMAC) is a major new initiative aimed at accelerating the adoption of fully continuous manufacturing processes for the quicker and more sustainable production of high-value, higher-quality chemicals such as pharmaceuticals at lower cost. To achieve this goal, CMAC's Director, pharmacist Professor Alastair Florence of the Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, leads a multidisciplinary team of academics from seven British universities and harnesses expertise from a wide range of scientific disciplines, including chemical and process engineering, chemistry, pharmaceutical science as well as manufacturing and operations management from across academia and industry. To date, CMAC has raised over £60 million from the Engineering and Physical Sciences Research Council together with input and support from CMAC's founding pharmaceutical industry partners, GlaxoSmithKline, AstraZeneca and Novartis. In recognition of his achievements, Prof. Florence was awarded the Royal Pharmaceutical Society Science Medal (2004) and was Conference Chair for the Academy of Pharmaceutical Sciences 2013 UKPharmSci conference.</p>	24
REGENERATIVE MEDICINE	<p>Regenerative medicine, i.e. replacing or regenerating human cells, tissues or organs to restore or establish normal function, holds the promise of regenerating damaged tissues and organs in the body. Pharmacist, Prof. Molly Stevens of Imperial College, London undertakes research into the directed differentiation of stem cells, the design of novel bioactive scaffolds, and new approaches towards tissue regeneration. To date, she has developed novel methods for engineering large quantities of human mature bone for autologous transplantation as well as other vital organs such as liver and pancreas. Efforts to commercialise the technologies have led to spin-out companies and the setting up of a clinical trial for bone regeneration in humans. Amongst the many awards Prof. Stevens has received is the Royal Pharmaceutical Society's 2007 Conference Science Medal. In 2004, she was recognised in the TR100 (the top 100 Young Innovators under the age of 35 who were transforming technology), while in 2010 she was named by The Times as one of the UK's top ten scientists under the age of 40.</p>	26

TITLE	VIGNETTE	PAGE
DEVELOPMENT OF AN ORALLY ACTIVE TREATMENT FOR THALASSAEMIA	Thalassaemia is the most prevalent inherited single-gene disorder in the world and life-saving therapy for this disease involves a combination of blood transfusion and iron chelation. Bob Hider, Professor of Medicinal Chemistry at King's College London, is a pharmaceutical scientist who is well known for his work in haematology. Prof. Hider designed the first orally active iron chelator, deferiprone (tradenames include Ferriprox). Prior to this orally active treatment, thalassaemia was treated using desferrioxamine, an iron chelating drug administered by continuous infusion over periods of 6–8 hours. Although deferiprone received approval from the EMA in 1999, it was not until 2011 that the FDA granted accelerated approval for the use of deferiprone in the USA. This decision – brought about largely as the result of extensive lobbying by patients – was made on the grounds that deferiprone satisfies an unmet need for a choice of iron chelation therapy for those patients in whom blood transfusion leads to potentially fatal cardiac iron burden. Deferiprone is increasingly being adopted by clinicians for the treatment of iron overload associated with the treatment of thalassaemia and sickle cell anaemia.	29
FORMULATION OF ANTI-CANCER THERAPIES	Chemotherapy is a mainstay of cancer treatment and the only therapeutic option for the treatment of disseminated disease. Led by the revolution in tumour biology, new drugs and new methods of administration of these drugs are currently being researched. Most of the new drugs considered are poorly water soluble and unstable, and so their translation into clinical therapies is critically dependent upon the application of pharmaceutical formulation skills combined with biopharmaceutical knowledge. Pharmacist Professor Gavin Halbert has been performing this translational role for 25 years at the Cancer Research UK Formulation Unit, achieving multiple successes (including temozolomide and abiraterone) and clinical leads for future research in areas such as targeted therapies and polymer therapeutics.	31
MICRONEEDLES	Novel drug delivery systems can enhance the clinical benefits of existing drugs and meet the challenge of delivering the new drugs of the future. Pharmaceutical scientists have a well-established track record in designing and developing innovative drug delivery systems that provide real benefits for patients. This is exemplified by the work of pharmacist Prof. Ryan Donnelly who is developing microneedles, arrays of tiny needles that painlessly, and without drawing blood, pierce the skin to facilitate delivery of vaccines, peptide and protein drugs and allow minimally invasive patient monitoring. The possibilities for microneedle-enhanced patient care are wide ranging. For example, those in the developing world are set to benefit from cheaper vaccination and premature babies from blood-free sampling of drug substances and biomarkers. Prof. Donnelly has received considerable recognition for his work, being the recipient of several prestigious awards, including the Royal Pharmaceutical Society's 2011 Science Award, the 2012 GSK Emerging Scientist Award and the BBSRC Innovator of the Year Award in 2013.	35

TITLE	VIGNETTE	PAGE
TAILORING THE DOSE OF A MEDICINE FOR A CHILD	Children are not small adults, and it is essential to understand that children's bodies respond to medicines in a different way than adults. Children need medicines that are tailored to their age, body weight and physiological condition. Until recently, only three broad age bands were used to define how much oral liquid paracetamol should be given to children between the ages of 3 months and 12 years. In 2011, the Medicines and Healthcare Products Regulatory Agency (MHRA) issued new dosage guidance that increased the number of age bands to 7, with a single dose per age band making it easier for parents and carers to know exactly how much paracetamol they should give their children.	40
GUIDELINES TO INCREASING DRUG EFFICACY	Obesity rates in the UK are the highest in Europe and have increased dramatically over the past few years. Obesity is fast becoming a major burden on the NHS. The management of infections in obese patients is problematic due to an increased risk of morbidity and mortality as well as a lack of information about dosing information. Pharmacists play an increasingly important role in the management of obese patients undergoing antimicrobial therapy because of the patients' altered pharmacokinetic handling of drugs. Optimising the efficacy and minimising the toxicity of antibiotics in this patient group requires a level of understanding of pharmacokinetic and pharmacodynamic principles that is uniquely provided by pharmacists. To date, only a few antibiotics, such as aminoglycosides, vancomycin, daptomycin and linezolid, have been sufficiently well studied in the obese population to allow recommendations to be made on altered dose. For some antibiotics, such as gentamicin and vancomycin, the use of ideal body weight or adjusted body weight rather than actual body weight is recommended, while for other antibiotics, including penicillins, cephalosporins, meropenem and aztreonam, a dose at the upper end of the recommended dosage range is proposed. ⁵⁸ Pharmacists have been instrumental in developing local guidelines to enable safer and more efficacious prescribing of these classes of drugs.	44
SHARED RECORD KEEPING AMONG HEALTHCARE PROFESSIONALS	Pharmacists often get requests for medicines out of GP hours when it is not possible to get access to the patient information that they need to help ensure they supply the right medicine. Pharmacists' access to patient records is pivotal to reducing medication errors, improving medicines adherence and ensuring the provision of safe and more effective care to patients. Scotland Patients Association recognises that increased roles for pharmacists within hospitals, primary care and the community should be an asset to patients and other health professionals, provided there is improved continuity of care for the patient and excellent communication between all health professionals. To achieve this will require accurate records to be kept and shared amongst health professionals, whilst maintaining patient confidentiality, and patients must be able to check their records for accuracy. In order to feel safe and confident, patients need to trust health professionals and sufficient time must be allotted to explain any new treatments or medication to patients. Pharmacists' access to a patient's medical record is crucial to improve patient safety through knowledge of an accurate patient diagnosis and all prescribed medicines.	45

TITLE	VIGNETTE	PAGE
THE SCOTTISH MEDICINES CONSORTIUM	<p>The purpose of the Scottish Medicines Consortium is to assess the evidence for clinical effectiveness and cost-effectiveness of newly licensed medicines, and to accept into routine use as quickly as possible those medicines that provide good value for money to NHS Scotland so that patients can benefit. To do this, the Consortium analyses information supplied by the drug manufacturer on the health benefits of the drug and the justification of its price. The Consortium is made up of clinicians, pharmacists and health economists together with representatives of health boards, the pharmaceutical industry and the public. The past chair of the Consortium is pharmacist Professor Angela Timoney, Director of Pharmacy at NHS Lothian. Pharmacists on the Consortium use their knowledge of pharmacoepidemiology, pharmacoconomics, public health, the critical appraisal of evidence and a statistical oversight, together with an awareness of the science behind systematic reviews and meta-analyses, to assess information supplied by medicines manufacturers on the health benefits provided by medicines and whether this justifies the associated cost.</p>	46
NHS NEW MEDICINE SERVICE	<p>The NHS New Medicine Service (NMS) in England, which started October 2011, is targeted to patients with long-term conditions that have been prescribed new medicines. It is anticipated that the NMS will lead to a variety of beneficial outcomes, including improved medicines adherence, reduced medicines wastage and an increased patient engagement with their condition and medicines, which will help them make decisions about their treatment and self-management. The NMS resulted directly from research on medicines adherence carried out by pharmacist Professor Nicholas Barber, Director of Research, The Health Foundation (formerly Professor of the Practice of Pharmacy, University College London). Indeed, much of Prof. Barber's research has focused on understanding what is currently wrong with things in order to establish how to do things better, then to introduce and evaluate services which should achieve this end. For example, Prof. Barber has evaluated electronic prescribing in primary care, automated dispensing systems, the prevalence and causes of prescribing errors in general practice, the implementation of the national Care Record Service in England and medication errors in nursing homes. The findings of these studies in medicines safety and behavioural medicine have influenced UK pharmacy practice and policy. In 2013, Prof. Barber and Dr Hamish Wilson published a 'Review of NHS Pharmaceutical Care of Patients in the Community in Scotland', a document that informed the Scottish Government's 'Prescription for Excellence: A Vision and Action Plan for the Right Pharmaceutical Care through Integrated Partnerships and Innovation.' Prof. Barber's work has been recognised in the award of the Guild of Healthcare Pharmacists' Gold Medal and a lifetime achievement award by the Royal Pharmaceutical Society.</p>	47

TITLE	VIGNETTE	PAGE
THE EFFECTS OF NON-COMPLIANCE	It is estimated that between 30-50% of patients who are prescribed medicines for chronic conditions do not take them as directed; this results in avoidable ill health and considerable economic loss to the healthcare system and indeed to society in general. Rob Horne, Professor of Behavioural Medicine, School of Pharmacy, University of London addressed this problem through a phased approach to developing effective interventions to non-adherence. Working with health psychologists, Prof. Horne developed a range of tools and models for assessing patient perspectives of illness and treatment, e.g. the Beliefs about Medicines Questionnaire (BMQ) and the Medication Adherence Report Scale (MARS), as well as frameworks (a Necessity-Concerns Framework) for understanding treatment-related behaviours with a particular focus on adherence to medication. This work translates into a portfolio of theory-based pragmatic interventions to help patients get the best from treatments by supporting optimal adherence and self-management. These tools balance the concerns people might have about the disadvantages of medicine taking against their beliefs in the medicine's effectiveness and contribute to the understanding of why medicines may or may not be taken by patients. ⁹⁹	50
RESPONSIBLE USE OF ANTIBIOTICS	It is essential that antibiotics are used responsibly, so that the right drug is provided at the right time, in the right dose and for the right duration. Too low a dose could result in killing the weaker bacteria, allowing stronger, more virulent bacteria to thrive. Although it is now widely recognised that the age-related average weight of children is much higher now than in the 1950s, the child dose of antibiotics has remained exactly the same over this period, resulting in significant under-dosing and thereby contributing to the development of antibiotic resistance. The penicillin V dosing regimens for children first appeared in 1963-1966 British National Formulary and have not been changed since, with the recommended single dose halving between successive age bands: child 12-18 years (500 mg), 6-12 years (250 mg), 1-5 years (125 mg), < 1 year (62.5 mg). In the same period, the adult dose has increased no less than four times.	54

TITLE	VIGNETTE	PAGE
MEDICINES USE IN AN OLDER POPULATION	<p>Currently, over 10 million people in the UK are over 65; this number is expected to increase to 19 million by 2050. These numbers are already placing considerable strain on social services and on residential care and nursing homes. Carmel Hughes, Professor of Primary Care Pharmacy, Queen's University Belfast focuses her research on the quality of drug use in older people, particularly in the long-term care setting. Her research has investigated the internal and external factors which influence prescribing, including adversarial legislation, organisational culture and multidisciplinary collaboration. This has led to the development of a unique pharmaceutical care intervention model. When tested in a cluster-randomised controlled trial, the model produced encouraging results, suggesting that the intervention was clinically effective and cost-effective. This intervention model has now been commissioned as part of a new service that will be made available to nursing homes across Northern Ireland. Prof. Hughes was the first pharmacist to be awarded a Harkness Fellowship in Health Care Policy from the Commonwealth Fund of New York City and a National Primary Care Career Scientist Award from the Research and Development Division of the DH. She was awarded the 2001 British Pharmaceutical Conference Medal. She has been a Cochrane Fellow, is a member of the Cochrane Collaboration and is Joint Clinical Lead for the Northern Ireland Clinical Research Network.</p>	55
THE MAUDSLEY PRESCRIBING GUIDELINES	<p>Mental illness is a growing problem in all areas of the world, affecting over a billion people at some point in their lives: lifetime risk of severe mental illness (schizophrenia and bipolar affective disorder) is 2.5%; depression 20% and anxiety 20%. Drug therapy is the mainstay of treatment in all of these conditions but prescribing is complex and optimal prescribing is rarely achieved. Professor David Taylor, Chief Pharmacist, South London and Maudsley, NHS Foundation Trust, London is lead editor of The Maudsley Prescribing Guidelines. These Guidelines which have been in continuous publication since 1994 are currently in their 11th Edition; they provide the only comprehensive evidence-based guide to psychotropic prescribing, and influence national and international prescribing. They are standard issue in the English-speaking world and have been translated into nine languages, to date selling more than 200,000 copies worldwide. Prof. Taylor's research programme provides data to support guidance within the publication. The current Guidelines include over 100 references to Prof. Taylor's work. The Guidelines represent the only comprehensive guide to evidence-based prescribing in mental illness in the world and are widely regarded as an essential text. The status of the Maudsley Prescribing Guidelines is such that other guideline bodies such as NICE make every effort to make their guidelines consistent with those in the Maudsley Guidelines.</p>	56

TITLE	VIGNETTE	PAGE
REDUCTION OF HOSPITAL SPREAD INFECTIONS	Clostridium difficile (C. difficile) is a bacterium that causes diarrhoea and more serious intestinal conditions such as colitis. C difficile infections most commonly occur in people who have recently had a course of antibiotics and are in hospital. In 2009, the Scottish Government set a target to reduce C. difficile infections in patients aged 65 and over by 30%, by reducing 4C prescribing (i.e. the prescribing of ciprofloxacin (and other quinolones), co-amoxiclav, cephalosporins, and clindamycin). In NHS Grampian, printed guidelines, posters, reminders on payslips, and root cause analysis of new C. difficile cases were used to implement change, with lead roles in this for antibiotic pharmacists and clinical pharmacists. As a result, 4C antibiotics, as a percentage of all prescribed oral antibiotics, dropped from approximately 40% to 15% and new C. difficile cases from 40 to 5 per month.	60
THE LIVEWELL INITIATIVE, NIGERIA	AIDS can be prevented by better education and removal of its associated social stigma. In Nigerian society, as indeed in the rest of Africa, Health literacy is very low. The LiveWell Initiative in Nigeria is a pharmacy-led educational project that aims to halve health-illiteracy in Nigeria by the year 2030, and thereby increase the life expectancy of Nigerians to 70 by the year 2030. Specifically the initiative aims to improve the health status of the Nigerian people through wellness promotion, health-empowerment and positive encouragement of health-seeking behaviour. The initiative aims to change the pleasure-seeking behaviour of youths and vulnerable adults by developing personal empowerment. The HIV/AIDS enlightenment programme to improve sexual health amongst the poor and vulnerable groups is just one of several initiatives which includes drug use and abuse, malaria eradication and illness poverty alleviation.	64
CONTRACT RESEARCH	The use of a contract research company to outsource a piece of development work is now common-place within the pharmaceutical industry. 30 years ago, however, the concept was virtually unheard off when pharmacist Sir Roger Jones spotted an opportunity to set-up a company to undertake contract development for the pharmaceutical industry. As a result he formed Penn Pharmaceuticals in 1979 in the village of Penn, Buckinghamshire, although the company now operates from South Wales. In addition to being one of the longest established contract companies in the world, Penn Pharmaceuticals has grown into one of the leading international contract research companies. Sir Roger has, more recently set up a variety of successful life science companies including Agroceutical Products Ltd (daffodil alkaloids), Bioextraction Wales Ltd (continuous countercurrent chromatography), Biofuels Wales Ltd (delignification), BioMonde Ltd, formerly ZooBiotic Ltd (maggot therapy) and Phytovation Ltd (natural products). Also realising the importance of staff training at the leading edge of technology Sir Roger, has also been active in the Training and Enterprise Councils, and was Chairman of Gwent Training and Enterprise Council. In recognition of his services to the pharmaceutical industry he received an OBE in 1996 and was Knighted in 2005. He was made a Fellow of the Royal Pharmaceutical Society in 2009.	68

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